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# BMJ Open

## Decreasing COVID-19 In-Hospital Mortality – Lessons from the Pandemic

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# Decreasing COVID-19 In-Hospital Mortality – Lessons from the Pandemic

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## Abstract

**Introduction:** COVID-19 first struck New York City in the spring of 2020 resulting in an unprecedented strain on our health care system triggering multiple changes in public health policy governing hospital operations as well as therapeutic approaches to COVID-19. We examined inpatient mortality at our center throughout the course of the pandemic.

**Methods:** Retrospective chart review of clinical characteristics, treatments, and outcome data of all patients admitted with COVID-19 from March 1<sup>st</sup>, 2020 to February 28<sup>th</sup>, 2021. Patients were grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds based on a normal bed capacity of 1,491.

**Results:** Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the year. During this time, the use of remdesivir, steroids, and anticoagulants increased; the use of hydroxychloroquine and other antibiotics decreased. Daily bed occupation ranged from 62% to 118% and COVID-19 mortality increased by 0.7% per 1% increase in bed occupation (HR 1.007, CI: 1.001, 1.013,  $p=0.004$ ). In a multivariate model with demographics, comorbidities, acuity of illness, and bed occupation inpatient mortality during the second surge remained significantly lower than during the initial surge (HR 0.520, CI 0.448-0.604,  $p<0.001$ ). Propensity score analysis confirmed this finding (HR 0.580 CI: 0.507-0.663,  $p<0.001$ ).

**Conclusion:** Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in disease specific therapeutics and was associated with bed occupation. Early reduction in epicenter hospital bed occupation to accommodate acutely ill and resource-intensive patients should be a critical component in the strategic planning for future pandemics.

### Strengths and limitations of this study

- Large cohort study (7,390 COVID-19 patients).
- Longitudinal analysis over 1 year of management and hospital policy changes.
- Analysis of mortality changes after adjustment for different therapies and clinical parameters.
- Identification of the association between level of hospital system stress and mortality, with important public health ramifications.
- Limitation: data on most recent variants are not included

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3 **Key questions:**  
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6 **What is already known?** COVID-19 treatment and mortality changed over one year. Was the  
7  
8 percentage of hospital bed occupation associated with in-patient mortality?  
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11 **What are the new findings?** In this retrospective cohort study of 7,390 COVID-19 patients  
12  
13 admitted to our institution over a 12-month period, we found that inpatient mortality due to  
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15 COVID-19 decreased to a degree disproportionate to advances in disease specific therapies.  
16  
17 Additionally, inpatient mortality due to COVID-19 was associated with the percentage of  
18  
19 hospital bed occupation.  
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23 **What do the new findings imply?** We provide important insights into the temporal changes in  
24  
25 COVID-19 prognosis and for the first time identify hospital stress – measured as the percentage  
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27 of bed occupation – as a parameter independently associated with COVID-19 mortality. Early  
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29 reductions in epicenter hospital bed occupation to accommodate acutely ill and resource-  
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31 intensive patients should be critical considerations in the strategic planning for future pandemics.  
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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization on March 11<sup>th</sup>, 2020.<sup>1</sup> In the United States, after a cluster of cases reported from Washington state<sup>2</sup>, New York state quickly became the initial epicenter of this pandemic with over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the Bronx and Queens boroughs of New York City.<sup>3</sup> Montefiore Einstein, with its three principal teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider for the large, nearly 1.5 million diverse population of the Bronx<sup>4</sup> and experienced a “first wave” of COVID-19 admissions in the spring of 2020<sup>3</sup>, followed by a significant reduction of cases until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course of the year, multiple public health measures - including those adapting hospital operation to a disaster level pandemic, such as cancellation of all elective procedures and waiver of state specific licensing for health care providers - were put in place. In addition, the understanding of COVID-19 pathophysiology improved<sup>5,6</sup>, new treatments were developed<sup>7-10</sup>, parts of the general population<sup>11,12</sup> as well as hospital personnel developed antibodies after COVID-19 illness<sup>13</sup>, and our hospital system adapted to and then recovered from crisis mode.<sup>14</sup> Here, we report outcomes of patients hospitalized with COVID-19 through one year since the first case, focusing on the differences observed between the spring and the winter surges.

## METHODS:

### Study Population

We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19



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3 between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month  
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5 seasons: spring (March 1, 2020 to May 31, 2020), summer (June 1, 2020 to August 30, 2020),  
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7 fall (September 1, 2020 to November 30, 2020), and winter (December 1, 2020 to February 28,  
8  
9 2021).  
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### 14 **Data Collection**

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17 Medical data including demographic, clinical, and laboratory variables were extracted from the  
18  
19 electronic medical record system. The primary outcome was 30-day in-hospital mortality.  
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### 24 **Statistical Analysis**

25  
26 Continuous variables are displayed as mean  $\pm$  standard deviation or median [25-75%  
27  
28 interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as  
29  
30 appropriate. Categorical data are presented as percent and compared by the chi-squared test. We  
31  
32 estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season,  
33  
34 treating hospital discharge as a competing event.<sup>15</sup> To avoid any bias due to differential follow-  
35  
36 up length, we censored the follow-up time at 30 days after the admission.  
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40 A multivariable competing risk proportional hazard models was used to estimate the sub-  
41  
42 distribution hazard ratios<sup>16 17</sup> for time to in-hospital death. Selection method for covariates is  
43  
44 presented in the Supplemental Material.  
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47 Then we focused on examining the difference in in-hospital death between patients admitted in  
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49 the spring and in the winter, as they represented the two largest and most temporal distant waves  
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51 of the COVID-19 pandemic occurring before and after pandemic specific therapeutic hospital  
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3 logistic changes had been implemented. Selection method for covariates is presented in the  
4  
5 Supplemental Material.  
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8 The proportionality assumption was examined<sup>18</sup> and no violation was identified. A two-sided  
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10  $p < 0.05$  was considered statistically significant.  
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### 14 15 **Propensity Score Analysis**

16  
17 To fully control the potential differences in patient population and hospital stress between spring  
18  
19 and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-  
20  
21 day in-hospital mortality between spring and winter admissions. The same covariates used for  
22  
23 the multivariable competing risk regression were used for PS matching. PS matching was carried  
24  
25 out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified  
26  
27 on matched pair in the competing risk regression model.<sup>19 20</sup> Because one-to-one matching led to  
28  
29 a reduction in sample size, we used this analysis as a sensitivity analysis.  
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33 All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R  
34  
35 packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)  
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### 40 41 **Patient and Public Involvement**

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43 Given the retrospective nature of our analysis, it was not appropriate or possible to involve  
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45 patients or the public in the design, or conduct, or reporting, or dissemination plans of our  
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47 research.  
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## 51 52 **RESULTS**

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3 7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28,  
4 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377  
5  
6 during the fall, and 2,254 during the winter.  
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9  
10 On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients  
11 admitted to our hospital (including those admitted to emergency adult wards at our children's  
12 hospital<sup>21</sup>) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19  
13  
14 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed  
15  
16 capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients.  
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19  
20 (**Figure 1**). Following cancellation of elective procedures, bed occupation decreased to 70% by  
21  
22 the end of the spring season and remained at 90% until the beginning of the winter season, when  
23  
24 the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the  
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26 beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%,  
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28 and 13%, respectively (**Figure 2**).  
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### 35 **Patient Population**

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37 Demographics, past medical history, vital signs at arrivals, and initial laboratory blood tests are  
38 presented in **Table 1**. Overall, median age was 66 (55 – 77) years, 3,835 (51.9%) patients were  
39  
40 male, 5,519 (74.2%) were of Black race and/or Hispanic ethnicity. Median age ranged from 63  
41  
42 years (fall) to 67 years (spring). Sex distribution was similar throughout the year. Summer and  
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44 fall patients had the lowest and the highest BMI: 26.7 and 28.6 kg/m<sup>2</sup>, respectively.  
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### 51 **Pharmacotherapy**

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53 Changes in pharmacological approach is presented in **Supplemental Table 1** and **Figure 3**  
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3 Spring patients were more likely to receive hydroxychloroquine, azithromycin and other  
4 antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2%  
5 during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during  
6 spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of  
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Spring patients were more likely to receive hydroxychloroquine, azithromycin and other antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2% during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also increased.

### Death, Intubation, and Length of Stay

Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older, had more comorbidities, and were more acutely ill consistent within prior reports on risk factors for death in COVID-19<sup>5 6</sup> (**Supplemental Table 2**). Average unadjusted monthly mortality is presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients ( $p < 0.001$ ). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival ( $p < 0.001$ ). Frequency of invasive ventilatory support was higher during the spring with 892 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268 (11.9%) in the winter,  $p < 0.001$ . Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients, and 2.8 (0.3 – 7.0) days for winter patients,  $p < 0.001$ . Median length of stay was 6.1 (3.5 – 11.1) days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and 6.3 (3.8 – 12.0) days during winter,  $p < 0.001$ .

### **Bed Saturation and Mortality**

In the multivariable competing risk proportional hazard model of the entire cohort, percent of bed occupation was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001, 1.013,  $p=0.004$ ); i.e mortality increase by 0.7 % for each 1% increase of bed occupation.

### **Spring vs Winter Mortality Comparison and Propensity Matched Analysis**

In the multivariable competing risk proportional hazard model comparing spring and winter season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604,  $p<0.001$ ) when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average difference among covariates was greatly reduced. PS analysis showed a significant reduction of in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663,  $p<0.001$ ) confirming what we observed in the multivariable adjusted analysis (**Figure 4B**).

### **DISCUSSION**

We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our hospital system in New York City. Our principal findings are as follows: First, we observed a substantial reduction of in-house mortality coinciding with multiple pandemic related public health measures focusing on hospital resources on COVID-19 – and preceding comprehensive changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the first time - hospital bed occupation as an independent risk factor for inpatient mortality from COVID-19.

## Public Health Measures in Response to COVID-19

After declaring a state of disaster emergency (March 7, 2020), New York State introduced different measures to limit the spread of the disease, including public schools closure (March 16, 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway closure (April 30, 2020)<sup>22</sup>. Despite these measures to limit the diffusion of the disease and a generalized reduction of movements around New York City (as evidenced by a more than 90% reduction of subway ridership compared to 2019)<sup>23</sup>, more than 30% of Bronx residents were found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2 in August 2020.<sup>24</sup>

Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)<sup>25</sup> allowed healthcare providers not licensed or registered in New York State to temporarily work in the State, and executive order no. 202.10 (March 22, 2020)<sup>25</sup> suspended elective operations. These executive orders were associated with a dramatic drop in non-COVID-19 admissions at our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to accommodate the surge of COVID-19 patients.<sup>25</sup> Despite this order, the actual bed occupation at our institution (while accommodating all COVID-19 patients presenting to our hospitals) remained below the usual operating capacity until December 2020.

Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although randomized controlled trials have shown morbidity benefits with the use of remdesivir<sup>7</sup> and

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3 mortality reduction with steroids<sup>8</sup>, the magnitude of these effects cannot explain the more than  
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5 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of  
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7 hydroxychloroquine elimination, did not materially change within the spring season, by the end  
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9 of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation  
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11 were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter  
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13 season. Despite that, unadjusted mortality began to increase again in December 2020 during the  
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15 second wave. Of note, bed occupation also increased at that time and proved to be an  
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17 independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.  
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### 24 **Change in Therapeutic Approach**

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26 The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent  
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28 eventually proven to be ineffective<sup>26</sup> to treat COVID-19, probably represents the most obvious  
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30 pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic  
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32 paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter  
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34 wave. To a similar extent, we observed a reduction in the use of azithromycin and other  
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36 antibiotics, the latter possibly reflecting a more careful assessment of the need to treat  
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38 superimposed bacterial infections during the second wave. Steroid therapy<sup>8,27</sup> and therapeutic  
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40 anticoagulation<sup>9</sup> were implemented in the majority of patients during the winter after the  
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42 knowledge on the likely disease modulating inflammatory proprieties and pro-thrombotic effect  
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44 of COVID-19 had been recognized<sup>28</sup> and, in the case of steroids, a therapeutic effect had been  
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46 proven<sup>8</sup>. Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase that showed  
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48 shortening of recovery time in hospitalized patients with COVID-19<sup>7</sup>, received emergency FDA  
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50 approval on October 22<sup>nd</sup>,2020<sup>29</sup> and was administered to almost half of the admitted patients  
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3 during the winter. If initial concerns of possible interactions between ACE-I or ARBs and  
4 SARS-CoV-2<sup>30</sup> led to a possible underutilization or discontinuation of these drugs during the  
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6 spring, we observed a significant increase in their use during the following months, after no  
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8 increased risks were reported.<sup>31 32</sup>  
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11 Similarly, after several reports showed a possible protective effect associated with the use of  
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13 statins<sup>33 34</sup>, their utilization markedly increased during the winter.  
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17 Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19  
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19 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was  
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21 developed to address respiratory distress in COVID-19; more data about such an approach has  
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23 since accumulated.<sup>10 35</sup>  
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### 28 **Change in Hospital Stress Load**

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30 At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed  
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32 capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in  
33  
34 acutely ill patients created significant excess demand on the rest of the hospital infrastructure  
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36 best characterized by the surge in the need for intensive care unit (ICU) beds and transformation  
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38 of other hospital areas to ICUs.<sup>14 21</sup> Despite increased patient load, the number of standard ICU  
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40 beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same  
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42 as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase  
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44 for each 1% increment in hospital bed saturation.  
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### 51 **Limitations**

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3 Our study has the shortcomings of a retrospective investigation, but there are some very specific  
4 aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of  
5 pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over  
6 the course of the year. Regardless, we believe the propensity-matched comparison between the  
7 spring and the winter waves provides compelling evidence for the validity of our principal  
8 observation of inpatient COVID-19 mortality reduction disproportionate to advances in  
9 pharmacotherapy. We chose total bed occupation as a metric for hospital stress assuming that  
10 other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19  
11 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably,  
12 an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis  
13 with disaster elements. Additionally, a significant number of patients received ICU-level-of-care  
14 interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors;  
15 therefore, the concept of ICU bed saturation might have been not truly representative of the  
16 burden.

17  
18 However, we feel our data is sufficiently strong to support the notion that bed capacity expansion  
19 alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by  
20 drastic reductions in all non-emergent procedures and activities is likely a better approach.

21  
22 Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in  
23 practice we observed that mortality began to decrease once beds and resources were allocated  
24 specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly  
25 that bed occupation never exceeded 100% once hospital operations focused on the COVID-19  
26 pandemic only. Lastly, it is conceivable that an uptrend in mortality observed late in the  
27 pandemic with established treatment paradigms could be due to new viral strains or a sicker

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3 patient population. Although we are unable to provide detailed strain analysis for our study  
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5 population, a meaningful numbers of new (and possibly more virulent) strains were not yet  
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7 observed in in the Bronx, where our study was conducted.<sup>36</sup> The small sample size of patients in  
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9 summer and fall does not allow meaningful propensity matched comparisons, and when  
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11 comparing summer, fall, and winter populations, there do not appear to be clinically meaningful  
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13 differences.  
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## 16 17 18 19 **CONCLUSIONS**

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21 Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in  
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23 disease specific therapeutics and was associated with bed occupation. Early reduction in  
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25 epicenter hospital bed occupation to accommodate acutely ill and resource-intensive patients  
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27 should be a critical component in the strategic planning for future pandemics.  
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## DECLARATIONS

### Ethics approval and consent to participate

The Office of Human Research Affairs at Albert Einstein College of Medicine approved this study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the retrospective nature of our research.

### Consent for publication

Non applicable.

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Competing interests

No conflicts of interest exist.

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### **Author's Contributions**

Design of the project: FC, XX, and UPJ.

Underlying data verified by FC, XX, and UPJ.

Acquisition, analysis, and interpretation of data: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Statistical analysis: FC and XX.

Obtained funding: UPJ

Manuscript writing: FC, XX, and UPJ.

Critical revision of the manuscript for important intellectual content: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS, and UPJ.

Supervision: UPJ

All the Authors reviewed the work and approved the final version.

FC and UPJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Not applicable

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**Table 1. Demographics, Past Medical History, and Clinical Characteristics of Admitted Patients**

	Spring (n=4495)		Summer (n=264)		Fall (n=377)		Winter (n=2254)	
	Sample	Value	Sample	Value	Sample	Value	Sample	Value
<b>Demographics</b>								
Age (IQR) - yr	4495	66 (55 - 77)	264	66 (50 - 76)	377	63 (50 - 73)	2254	67 (56 - 77)
Male sex - no (%)	4495	2377 (52.9)	264	138 (52.3)	377	198 (52.5)	2254	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	264	219 (83.0)	377	286 (75.9)	2254	1635 (74.2)
Body Mass Index (IQR) - kg/m <sup>2</sup>	4229	28.4 (24.6 - 33)	250	27.6 (22.5 - 32.7)	358	28.6 (25 - 34.1)	2194	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	264	81.7 (76.3 – 85.8)	377	87.6 (83.2 - 90.2)	2254	95.3 (91.9 – 101.8)
<b>Past Medical History</b>								
Hypertension - no (%)	4495	3370 (75)	264	197 (74.6)	377	254 (67.4)	2254	1713 (76)
Sleep apnea - no (%)	4495	521 (11.6)	264	28 (10.6)	377	47 (12.5)	2254	270 (12)
Hyperlipidemia - no (%)	4495	2609 (58)	264	153 (58)	377	199 (52.8)	2254	1380 (61.2)
Atrial fibrillation - no (%)	4495	449 (10)	264	30 (11.4)	377	35 (9.3)	2254	267 (11.8)
Chronic kidney disease - no (%)	4495	1406 (31.3)	264	70 (26.5)	377	85 (22.5)	2254	620 (27.5)
Heart failure - no (%)	4495	980 (21.8)	264	72 (27.3)	377	66 (17.5)	2254	519 (23)
Coronary artery disease - no (%)	4495	1316 (29.3)	264	95 (36)	377	108 (28.6)	2254	721 (32)
Asthma/COPD - no (%)	4495	1371 (30.5)	264	84 (31.8)	377	98 (26)	2254	753 (33.4)
Diabetes mellitus - no (%)	4495	2522 (56.1)	264	148 (56.1)	377	187 (49.6)	2254	1244 (55.2)



<b>Vitals at Presentation</b>								
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	264	98.4 (97.8 - 98.9)	372	98.8 (98.1 - 99.9)	2254	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	4469	131 (114 - 148)	264	132 (117 - 149)	375	131 (117 - 147)	2254	132 (117 - 148)
DBP (IQR) - mmHg	4465	75 (65 - 84)	263	77 (67 - 87)	374	74 (68 - 84)	2252	75 (67 - 84)
HR (IQR) – bpm	4467	98 (85 - 112)	264	92.5 (76.3 - 105)	372	94 (80 - 107)	2253	95 (82 - 107)
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	264	98 (96 - 99)	372	96 (94 - 98)	2253	96 (92 - 98)
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	264	18 (17 - 20)	372	18 (18 - 20)	2254	19 (18 - 22)
<b>Laboratory Markers</b>								
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	261	12.4 (10.7 - 13.9)	370	13 (11.6 - 14.3)	2228	12.9 (11.5 - 14.2)
Platelet count (IQR) -k/ $\mu$ L	4372	188 (116 - 260)	261	228 (169 - 300)	372	200 (144 - 257)	2228	196 (143 - 259)
White blood cell count (IQR) - k/ $\mu$ L	4372	7.5 (5.6 - 10.6)	261	8 (5.8 - 11)	370	6.6 (5.1 - 8.9)	2228	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/ $\mu$ L	4420	1 (0.7 - 1.4)	263	1.2 (0.9 - 1.8)	374	1.1 (0.8 - 1.5)	2246	1 (0.7 - 1.4)
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	263	138 (135 - 141)	377	137 (135 - 140)	2253	137 (134 - 140)
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	262	4.2 (3.8 - 4.6)	377	4 (3.8 - 4.4)	2243	4.1 (3.8 - 4.5)
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	263	103 (100 - 105)	377	101 (99 - 104)	2253	101 (98 - 104)
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	263	24 (21 - 27)	377	25 (22 - 27)	2253	24 (21 - 27)
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	263	1 (0.8 - 1.5)	377	1 (0.8 - 1.3)	2253	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	263	121 (100 - 171)	377	122 (102 - 173)	2253	126 (104 - 184)

Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	245	26 (20 - 38)	354	31 (21 - 47)	2084	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	252	21 (14 - 32)	361	25 (16 - 41)	2171	26 (17 - 44)
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	220	1.9 (1.4 - 2.7)	330	1.8 (1.3 - 2.5)	1913	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	160	254.5 (196 - 340)	285	300 (225 - 383)	1563	341 (254 - 468)
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	209	97 (57 - 176)	313	116 (60 - 213)	1957	126 (67 - 282)
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	185	1.1 (0.5 - 2.2)	317	0.8 (0.5 - 1.6)	1907	1.2 (0.7 - 2.3)
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	120	0.1 (0.1 - 0.4)	254	0.1 (0.1 - 0.2)	1252	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	0	NA	219	0.01 (0.01 - 0.03)	342	0.01 (0.01 - 0.02)	2106	0.01 (0.01 - 0.03)
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	3	0.01 (0.01 - 0.01)	0	NA	0	NA
Interleukin-6 (IQR) – pg/mL	1056	33.6 (13.8 - 75.2)	87	11.7 (3 - 43.1)	186	11 (4.7 - 22.2)	710	10.8 (4.3 - 25.6)
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	122	448 (370- 583)	224	540 (436 - 663)	1040	535.5 (434 - 652)
Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	155	228 (90 - 562)	293	364 (166 - 785)	1637	510 (230 - 1094)

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

## Figure Legends

### Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

### Figure 2. Cumulative Monthly Admission and Mortality

Cumulative monthly admissions (blue line, left axis) and mortality (orange line, right axis) over the year.

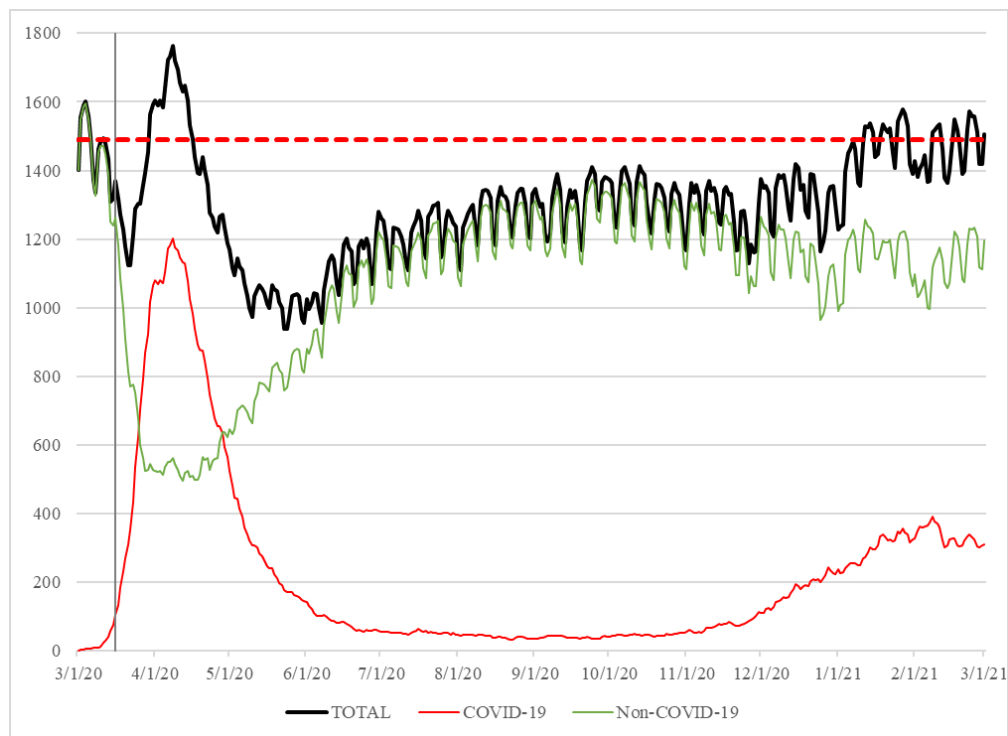
### Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

### Figure 4. Cumulative Incidences

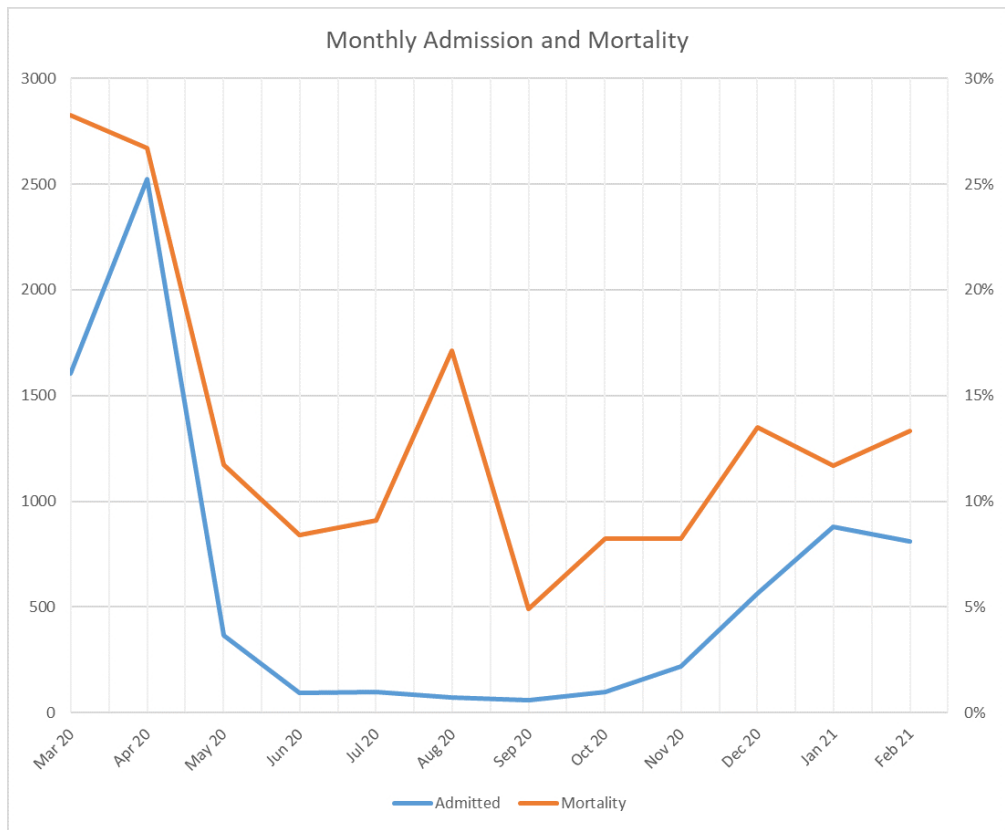
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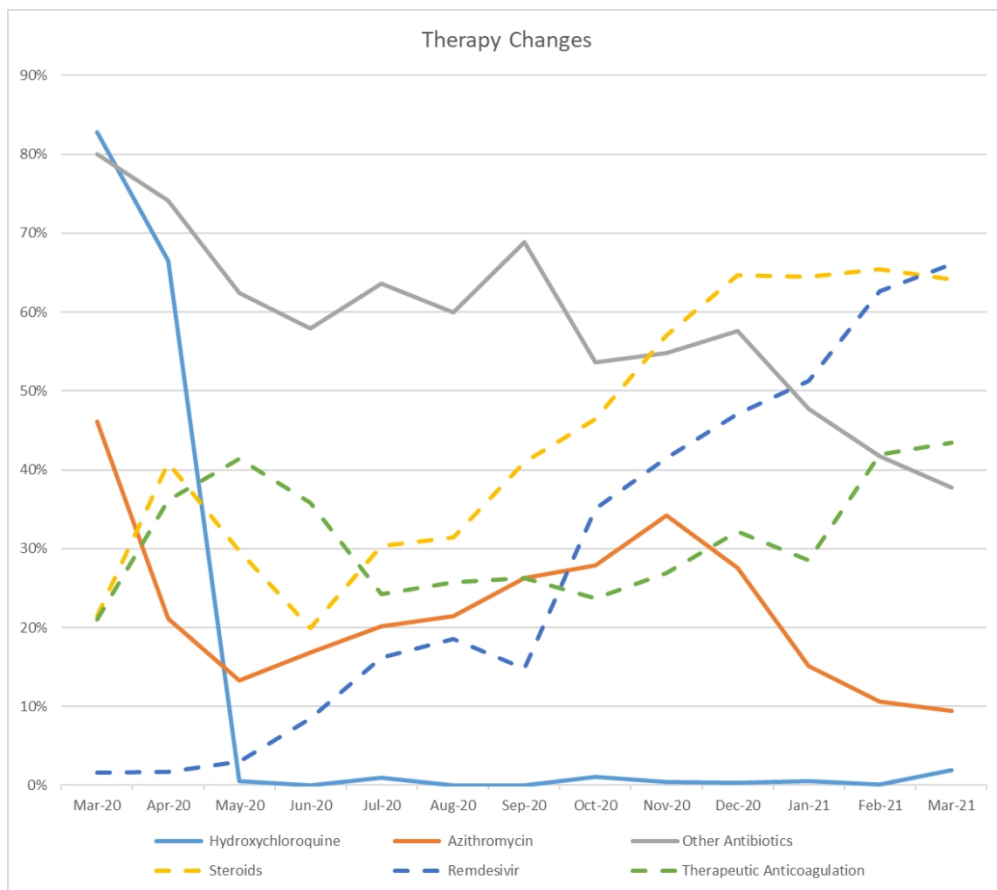
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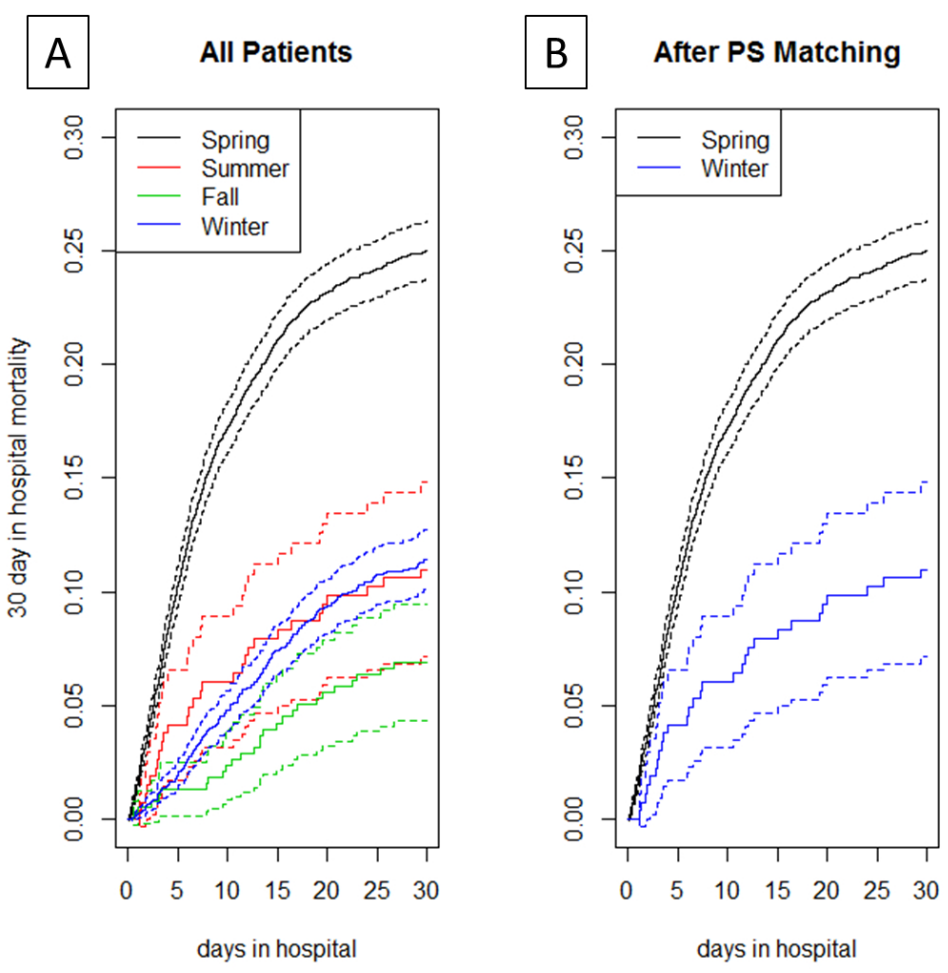
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For peer review only



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## Supplemental Methods

### *Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for Time to In-hospital Death*

The covariates in the multivariable analyses included factors present in > 90% of our dataset, known to be associated with in-hospital COVID-19 mortality based on prior literature<sup>1-3</sup>, or with a univariate association with in-hospital mortality ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between survivors and non survivors (**Supplemental Table 2**). These variables included: age, sex, body mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure, heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium, bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

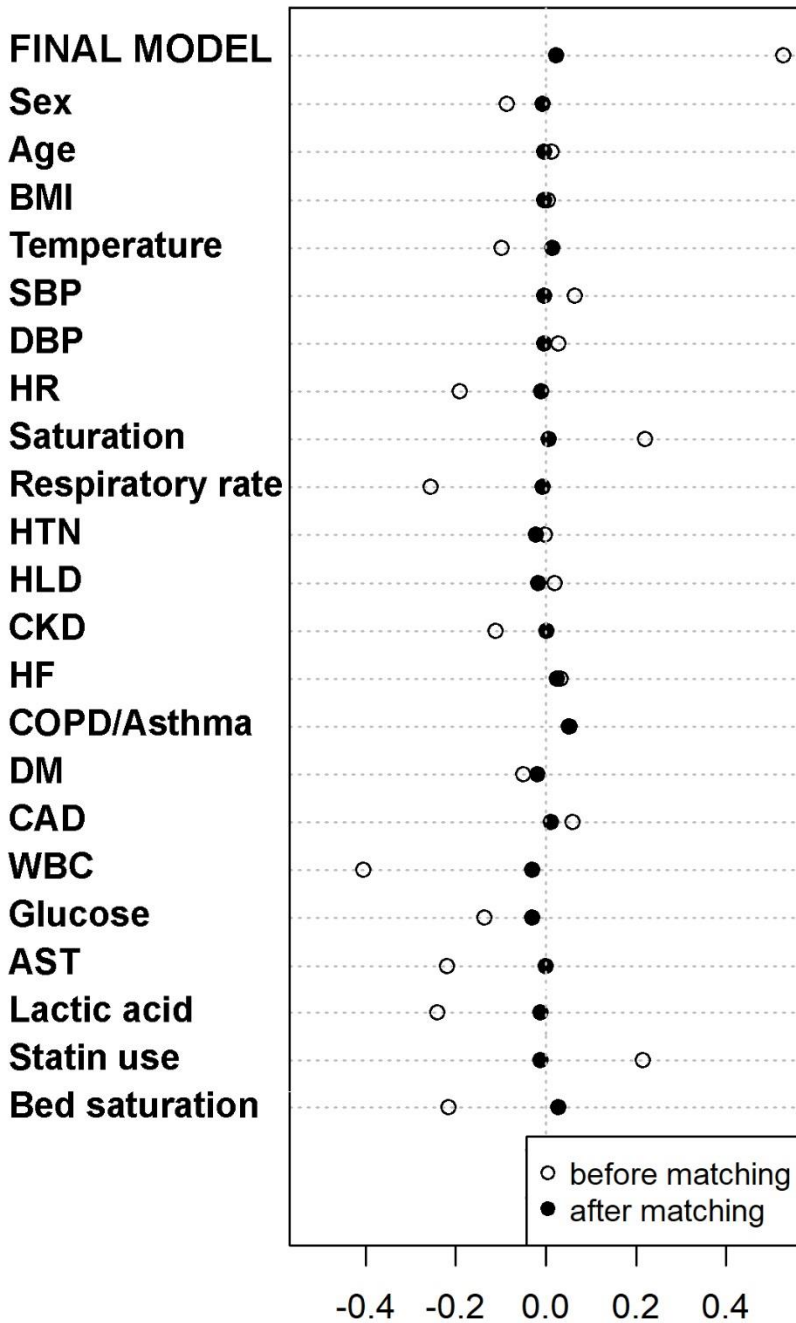
### *Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients*

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 3**). These variables included: age, sex, BMI, vital signs at

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3 presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension,  
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5 dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease,  
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7 asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this  
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9 model, lactic acid level and percent of hospital bed saturation were forced into the model as  
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11 marker of illness severity and level of hospital stress, respectively.  
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Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

**Supplemental Table 1 - Therapies Administered during the Admission**

	<b>Spring (n=4495)</b>	<b>Summer (n=264)</b>	<b>Fall (n=377)</b>	<b>Winter (n=2254)</b>
<b>Hydroxychloroquine - no (%)</b>	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
<b>Azithromycin - no (%)</b>	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
<b>Other antibiotics - no (%)</b>	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
<b>Steroids - no (%)</b>	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
<b>Angiotensin-converting-enzyme Inhibitors - no (%)</b>	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
<b>Angiotensin II receptor blockers - no (%)</b>	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
<b>Statin - no (%)</b>	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
<b>Therapeutic anticoagulation - no (%)</b>	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
<b>Remdesivir* - no (%)</b>	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
<b>Lopinavir/Ritonavir – no (%)</b>	40 (0.9)	0 (0)	0 (0)	0 (0)
<b>Ivermectin – no (%)</b>	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

\* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.

**Supplemental Table 2 - Comparison Survivors versus Nonsurvivors**

	Survivors (n=5953)		Nonsurvivors (n=1437)		p-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity – no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m <sup>2</sup>	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35

SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001
DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001
Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
<b>Laboratory Markers</b>					
Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
Platelet count (IQR) -k/ $\mu$ L	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
White blood cell count (IQR) - k/ $\mu$ L	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
Absolute lymphocyte count (IQR) - k/ $\mu$ L	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	4017	384 $\pm$ 219	926	518 (371 - 706)	<0.001
Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777 $\pm$ 2657	<0.001
D-dimer (IQR) - $\mu$ g/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001

Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
Troponin I* (IQR) - ng/mL	2684	0.01 (0.01 - 0.02)	981	0.02 (0.01 - 0.08)	<0.001
Interleukin-6 (IQR) - pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
Fibrinogen (IQR) - mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001
Ferritin (IQR) - ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.



**Supplemental Table 3 - Comparison Spring Vs Winter**

	Spring (n=4495)		Winter (n=2254)		P-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m <sup>2</sup>	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	2254	95.3 (91.9 – 101.8)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001

SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) – bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
<b>Laboratory Markers</b>					
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
Platelet count (IQR) -k/ $\mu$ L	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
White blood cell count (IQR) - k/ $\mu$ L	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
Absolute lymphocyte count (IQR) - k/ $\mu$ L	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
D-dimer (IQR) - $\mu$ g/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001

Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001
Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

## Supplemental References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *Jama* 2020;323:1239-42.
2. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584:430-6.
3. Tartof SY, Qian L, Hong V, et al. Obesity and Mortality Among Patients Diagnosed With COVID-19: Results From an Integrated Health Care Organization. *Ann Intern Med* 2020;173:773-81.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12- 13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5-6  Supp
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	6-7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	6-9
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-9
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
5	<b>Discussion</b>			
6	Key results	18	Summarise key results with reference to study objectives	9
7	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
8	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
9	Generalisability	21	Discuss the generalisability (external validity) of the study results	14
10	<b>Other information</b>			
11	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Impact of COVID-19 Pandemic Management on Outcomes in a Large United States Hospital Center

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# Impact of COVID-19 Pandemic Management on Outcomes in a Large United States Hospital Center

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## 28 **Abstract**

29 **Introduction:** COVID-19 first struck New York City in the spring of 2020 resulting in an  
30 unprecedented strain on our health care system triggering multiple changes in public health  
31 policy governing hospital operations as well as therapeutic approaches to COVID-19. We  
32 examined inpatient mortality at our center throughout the course of the pandemic.

33 **Methods:** Retrospective chart review of clinical characteristics, treatments, and outcome data of  
34 all patients admitted with COVID-19 from March 1<sup>st</sup>, 2020 to February 28<sup>th</sup>, 2021. Patients were  
35 grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds  
36 based on a normal bed capacity of 1,491.

37 **Results:** Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the  
38 year. During this time, the use of remdesivir, steroids, and anticoagulants increased; the use of  
39 hydroxychloroquine and other antibiotics decreased. Daily bed occupancy ranged from 62% to  
40 118% occupancy. In a multivariate model with all year's data controlling for demographics,  
41 comorbidities, and acuity of illness, bed occupancy was associated with an increased COVID-19  
42 mortality. Yet further adjustment of bed occupancy showed a significant lower mortality rate  
43 during the second surge compared to the initial surge (HR 0.520, CI 0.448-0.604,  $p < 0.001$ ).  
44 Propensity score analysis confirmed this difference in these two seasons (HR 0.580 CI: 0.507-  
45 0.663,  $p < 0.001$ ).

46 **Conclusion:** Inpatient mortality from COVID-19 decreased to a degree disproportionate to  
47 advances in disease specific therapeutics and was associated with bed occupancy. Early  
48 reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive  
49 patients should be a critical component in the strategic planning for future pandemics.

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2  
3 50 **Strengths and limitations of this study**  
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5

- 6 51 • Large cohort study (7,390 COVID-19 patients).  
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8 52 • Longitudinal analysis over 1 year of management and hospital policy changes.  
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11 53 • Analysis of mortality changes after adjustment for different therapies and clinical  
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13 54 parameters.  
14  
15 55 • Identification of the association between level of hospital system stress and mortality,  
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17 with important public health ramifications.  
18 56  
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20 57 • Limitation: data on most recent variants are not included  
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## 59 INTRODUCTION

60 Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health  
61 Organization on March 11<sup>th</sup>, 2020.<sup>1</sup> In the United States, after a cluster of cases reported from  
62 Washington state<sup>2</sup>, New York state quickly became the initial epicenter of this pandemic with  
63 over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the  
64 Bronx and Queens boroughs of New York City.<sup>3</sup> Montefiore Einstein, with its three principal  
65 teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider  
66 for the large, nearly 1.5 million diverse population of the Bronx<sup>4</sup> and experienced a “first wave”  
67 of COVID-19 admissions in the spring of 2020<sup>3</sup>, followed by a significant reduction of cases  
68 until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course  
69 of the year, multiple public health measures - including those adapting hospital operation to a  
70 disaster level pandemic, such as cancellation of all elective procedures and waiver of state  
71 specific licensing for health care providers - were put in place. In addition, the understanding of  
72 COVID-19 pathophysiology improved<sup>5,6</sup>, new treatments were developed<sup>7-10</sup>, parts of the  
73 general population<sup>11,12</sup> as well as hospital personnel developed antibodies after COVID-19  
74 illness<sup>13</sup>, and our hospital system adapted to and then recovered from crisis mode.<sup>14</sup> Here, we  
75 report outcomes of patients hospitalized with COVID-19 through one year since the first case,  
76 focusing on the differences observed between the spring and the winter surges.

## 78 METHODS:

### 79 Study Population

80 We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real  
81 time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19

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3 82 between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month  
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5 83 seasons based on northern hemisphere calendar: spring (March 1, 2020 to May 31, 2020),  
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7 84 summer (June 1, 2020 to August 30, 2020), fall (September 1, 2020 to November 30, 2020), and  
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9 85 winter (December 1, 2020 to February 28, 2021).  
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## 14 87 **Data Collection**

15  
16  
17 88 Medical data including demographic, clinical, and laboratory variables were extracted from the  
18  
19 89 electronic medical record system. The primary outcome was 30-day in-hospital mortality.  
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## 23 91 **Statistical Analysis**

24  
25  
26 92 Continuous variables are displayed as mean  $\pm$  standard deviation or median [25-75%  
27  
28 93 interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as  
29  
30  
31 94 appropriate. Categorical data are presented as percent and compared by the chi-squared test. We  
32  
33 95 estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season,  
34  
35 96 treating hospital discharge as a competing event.<sup>15</sup> To avoid any bias due to differential follow-  
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37 97 up length, we censored the follow-up time at 30 days after the admission.

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39  
40 98 A multivariable competing risk proportional hazard models was used to estimate the sub-  
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42 99 distribution hazard ratios<sup>16 17</sup> for time to in-hospital death. The covariates in the multivariable  
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45 100 analyses included factors present in > 90% of our dataset, known to be associated with in-  
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47 101 hospital COVID-19 mortality based on prior literature<sup>6 18 19</sup>, or with a univariate association with  
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49 102 in-hospital mortality ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between  
50  
51 103 survivors and non survivors (**Supplemental Table 1**). These variables included: age, sex, body  
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54 104 mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure,  
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3 105 heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium,  
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5 106 bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of  
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7 107 hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease,  
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10 108 asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally,  
11  
12 109 lactic acid level and percent of hospital bed saturation were forced into the model as marker of  
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14  
15 110 illness severity and level of hospital stress, respectively.  
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18 111  
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20 112 Then we focused on examining the difference in in-hospital death between patients admitted in  
21  
22 113 the spring and in the winter, as they represented the two largest and most temporal distant waves  
23  
24 114 of the COVID-19 pandemic occurring before and after public health polices, specific therapeutic  
25  
26 115 approaches and hospital management changes had been implemented. Selection method for  
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28  
29 116 covariates is presented in the **Supplemental Material** and **Supplemental Table 2**.

30  
31 117 The proportionality assumption was examined<sup>20</sup> and no violation was identified. A two-sided  
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33  
34 118  $p < 0.05$  was considered statistically significant.  
35

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### 38 120 **Propensity Score Analysis**

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40  
41 121 To fully control the potential differences in patient population and hospital stress between spring  
42  
43 122 and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-  
44  
45 123 day in-hospital mortality between spring and winter admissions. The same covariates used for  
46  
47 124 the multivariable competing risk regression were used for PS matching. PS matching was carried  
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49  
50 125 out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified  
51  
52 126 on matched pair in the competing risk regression model.<sup>21 22</sup> Because one-to-one matching led to  
53  
54 127 a reduction in sample size, we used this analysis as a sensitivity analysis.  
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3 128 All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R  
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5 129 packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)  
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### 10 131 **Patient and Public Involvement**

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12 132 Given the retrospective nature of our analysis, it was not appropriate or possible to involve  
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14 133 patients or the public in the design, or conduct, or reporting, or dissemination plans of our  
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16 134 research.  
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### 21 136 **RESULTS**

22  
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24 137 7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28,  
25  
26 138 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377  
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28 139 during the fall, and 2,254 during the winter.

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31 140 On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients  
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33 141 admitted to our hospital (including those admitted to emergency adult wards at our children's  
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35 142 hospital<sup>23</sup>) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19  
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37 143 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed  
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39 144 capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients.

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42 145 (**Figure 1**). Following cancellation of elective procedures, bed occupancy decreased to 70% by  
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44 146 the end of the spring season and remained at 90% until the beginning of the winter season, when  
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46 147 the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the  
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48 148 beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%,  
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50 149 and 13%, respectively (**Figure 2**).  
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## 151 **Patient Population**

152 Demographics, past medical history, vital signs at arrivals, and initial laboratory blood tests are  
153 presented in **Table 1**. Overall, median age was 66 (55 – 77) years, 3,835 (51.9%) patients were  
154 male, 5,519 (74.2%) were of Black race and/or Hispanic ethnicity. Median age ranged from 63  
155 years (fall) to 67 years (spring). Sex distribution was similar throughout the year. Summer and  
156 fall patients had the lowest and the highest BMI: 26.7 and 28.6 kg/m<sup>2</sup>, respectively.

## 158 **Pharmacotherapy**

159 Changes in pharmacological approach is presented in **Supplemental Table 3** and **Figure 3**.  
160 Spring patients were more likely to receive hydroxychloroquine, azithromycin and other  
161 antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2%  
162 during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during  
163 spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of  
164 statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also  
165 increased.

## 167 **Death, Intubation, and Length of Stay**

168 Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older,  
169 had more comorbidities, and were more acutely ill consistent within prior reports on risk factors  
170 for death in COVID-19<sup>5 6</sup> (**Supplemental Table 1**). Average unadjusted monthly mortality is  
171 presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring  
172 patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients  
173 (p<0.001). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the



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3 174 emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4  
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5 175 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival  
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7 176 ( $p < 0.001$ ). Frequency of invasive ventilatory support was higher during the spring with 892  
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9 177 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268  
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11 178 (11.9%) in the winter,  $p < 0.001$ . Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days  
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13 179 for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients,  
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15 180 and 2.8 (0.3 – 7.0) days for winter patients,  $p < 0.001$ . Median length of stay was 6.1 (3.5 – 11.1)  
16  
17 181 days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and  
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19 182 6.3 (3.8 – 12.0) days during winter,  $p < 0.001$ .  
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### 26 184 **Bed Saturation and Mortality**

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28 185 We defined bed saturation the percentage of bed occupancy calculated from the ratio between the  
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30 186 number of admitted patients over the nominal bed capacity of our institution (1,491).

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33 187 In the multivariable competing risk proportional hazard model of the entire cohort, percent of  
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35 188 bed occupancy was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001,  
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37 189 1.013,  $p = 0.004$ ); i.e mortality increase by 0.7 % for each 1% increase of bed occupancy.

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39 190 Consistent results were observed per level increase in bed occupancy quartile, (HR 1.086 [1.026  
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41 -1.148], P-value for linear trend = 0.004). Results of the competing risk regression analysis are  
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43 191 presented in the **Table 2**.  
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### 47 193 48 49 194 **Spring vs Winter Mortality Comparison and Propensity Matched Analysis**

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51 195 In the multivariable competing risk proportional hazard model comparing spring and winter  
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53 196 season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604,  $p < 0.001$ )  
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3 197 when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and  
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5 198 winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average  
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7 199 difference among covariates was greatly reduced. PS analysis showed a significant reduction of  
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9 200 in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663,  $p < 0.001$ ) confirming what we  
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11 201 observed in the multivariable adjusted analysis (**Figure 4B**).

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## 16 17 203 **DISCUSSION**

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19 204 We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our  
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21 205 hospital system in New York City. Our principal findings are as follows: First, we observed a  
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23 206 substantial reduction of in-hospital mortality coinciding with multiple pandemic related public  
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25 207 health measures focusing on hospital resources on COVID-19 – and preceding comprehensive  
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27 208 changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the  
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29 209 first time - hospital bed occupancy as an independent risk factor for inpatient mortality from  
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31 210 COVID-19.

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### 36 37 212 **Public Health Measures in Response to COVID-19**

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39 213 After declaring a state of disaster emergency (March 7, 2020), New York State introduced  
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41 214 different measures to limit the spread of the disease, including public schools closure (March 16,  
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43 215 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers  
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45 216 (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway  
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47 217 closure (April 30, 2020)<sup>24</sup>. Despite these measures to limit the diffusion of the disease and a  
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49 218 generalized reduction of movements around New York City (as evidenced by a more than 90%  
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51 219 reduction of subway ridership compared to 2019)<sup>25</sup>, more than 30% of Bronx residents were

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3 220 found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2  
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5 221 in August 2020.<sup>26</sup>  
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8 222 Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)<sup>27</sup>  
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10 223 allowed healthcare providers not licensed or registered in New York State to temporarily work in  
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12 224 the State, and executive order no. 202.10 (March 22, 2020)<sup>27</sup> suspended elective operations.  
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14 225 These executive orders were associated with a dramatic drop in non-COVID-19 admissions at  
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16 226 our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State  
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18 227 Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to  
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20 228 accommodate the surge of COVID-19 patients.<sup>27</sup> Despite this order, the actual bed occupancy at  
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22 229 our institution (while accommodating all COVID-19 patients presenting to our hospitals)  
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24 230 remained below the usual operating capacity until December 2020.  
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27 231 Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low  
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29 232 case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although  
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31 233 randomized controlled trials have shown morbidity benefits with the use of remdesivir<sup>7</sup> and  
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33 234 mortality reduction with steroids<sup>8</sup>, the magnitude of these effects cannot explain the more than  
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35 235 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of  
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37 236 hydroxychloroquine elimination, did not materially change within the spring season, by the end  
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39 237 of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation  
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41 238 were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter  
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43 239 season. Despite that, unadjusted mortality began to increase again in December 2020 during the  
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45 240 second wave. Of note, bed occupancy also increased at that time and proved to be an  
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47 241 independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.  
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### 243 **Change in Therapeutic Approach**

244 The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent  
245 eventually proven to be ineffective<sup>28</sup> to treat COVID-19, probably represents the most obvious  
246 pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic  
247 paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter  
248 wave. Similarly, we observed a reduction in the use of azithromycin and other antibiotics, the  
249 latter possibly reflecting a more careful assessment of the need to treat superimposed bacterial  
250 infections during the second wave. Steroid therapy<sup>8,29</sup> and therapeutic anticoagulation<sup>9</sup> were  
251 implemented in the majority of patients during the winter after the knowledge on the likely  
252 disease modulating inflammatory properties and pro-thrombotic effect of COVID-19 had been  
253 recognized<sup>30</sup> and, in the case of steroids, a therapeutic effect had been proven<sup>8</sup>. Remdesivir, an  
254 inhibitor of the viral RNA-dependent RNA polymerase that showed shortening of recovery time  
255 in hospitalized patients with COVID-19<sup>7</sup>, received emergency FDA approval on October  
256 22<sup>nd</sup>, 2020<sup>31</sup> and was administered to almost half of the admitted patients during the winter. If  
257 initial concerns of possible interactions between ACE-I or ARBs and SARS-CoV-2<sup>32</sup> led to a  
258 possible underutilization or discontinuation of these drugs during the spring, we observed a  
259 significant increase in their use during the following months, after no increased risks were  
260 reported.<sup>33,34</sup>

261 Similarly, after several reports showed a possible protective effect associated with the use of  
262 statins<sup>35,36</sup>, their utilization markedly increased during the winter.

263 Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19  
264 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was  
265 developed to address respiratory distress in COVID-19; more data about such an approach has

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3 266 since accumulated.<sup>10 37</sup> The cumulative effect of these therapeutic changes, in combination with  
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5 267 a better preparedness to respond to a pandemic, can be estimate from the different mortality  
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7 268 between the first surge (spring) and the second surge (winter). After matching the two groups for  
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9 269 demographic and clinical variables, as well as for elements indicative of hospital distress (bed  
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11 270 occupancy), a significant reduction of mortality was observed during the winter trimester.  
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### 16 17 272 **Change in Hospital Stress Load**

18  
19 273 At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed  
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21 274 capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in  
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23 275 acutely ill patients created significant excess demand on the rest of the hospital infrastructure  
24  
25 276 best characterized by the surge in the need for intensive care unit (ICU) beds and transformation  
26  
27 277 of other hospital areas to ICUs.<sup>14 23</sup> Despite increased patient load, the number of standard ICU  
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29 278 beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same  
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31 279 as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase  
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33 280 for each 1% increment in hospital bed saturation. In light of these results, strategies to minimize  
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35 281 the bed occupancy for non-Covid-19 patients or non-life-saving admission should be adopted to  
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37 282 diverge resources to improve the outcome of admitted Covid-19 patients.  
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### 44 284 **Limitations**

45  
46 285 Our study has the shortcomings of a retrospective investigation, but there are some very specific  
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48 286 aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of  
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50 287 pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over  
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52 288 the course of the year. Regardless, we believe the propensity-matched comparison between the  
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3 289 spring and the winter waves provides compelling evidence for the validity of our principal  
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5 290 observation of inpatient COVID-19 mortality reduction disproportionate to advances in  
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7 291 pharmacotherapy. We chose total bed occupancy as a metric for hospital stress assuming that  
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9 292 other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19  
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11 293 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably,  
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13 294 an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis  
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15 295 with disaster elements. Additionally, a significant number of patients received ICU-level-of-care  
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17 296 interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors;  
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19 297 therefore, the concept of ICU bed saturation might have been not truly representative of the  
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21 298 burden.

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26 299 However, we feel our data is sufficiently strong to support the notion that bed capacity expansion  
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28 300 alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by  
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30 301 drastic reductions in all non-emergent procedures and activities is likely a better approach.

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33 302 Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in  
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35 303 practice we observed that mortality began to decrease once beds and resources were allocated  
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37 304 specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly  
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39 305 that bed occupancy never exceeded 100% once hospital operations focused on the COVID-19  
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41 306 pandemic only. It is conceivable that an uptrend in mortality observed late in the pandemic with  
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43 307 established treatment paradigms could be due to new viral strains or a sicker patient population.

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45 308 Although we are unable to provide detailed strain analysis for our study population, a meaningful  
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47 309 numbers of new (and possibly more virulent) strains were not yet observed in in the Bronx,  
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49 310 where our study was conducted.<sup>38</sup> The small sample size of patients in summer and fall does not  
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51 311 allow meaningful propensity matched comparisons, and when comparing summer, fall, and  
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3 312 winter populations, there do not appear to be clinically meaningful differences. Lastly, single-  
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5 313 patient data on vaccination status were not available. At the conclusion of the study, only 13.8%  
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7 314 of the population of New York State received at least one dose and 7.4% received two doses<sup>39</sup>.  
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9 315 Given the heterogeneous distribution of vaccination within the state (and the city of New York),  
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11 316 it is impossible to meaningfully account for these parameters.  
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## 16 318 **CONCLUSIONS**

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19 319 Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in  
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21 320 disease specific therapeutics and was associated with bed occupancy. Early reduction in  
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23 321 epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive patients  
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25 322 should be a critical component in the strategic planning for future pandemics.  
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3 **325 DECLARATIONS**  
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5  
6 **326 Ethics approval and consent to participate**  
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8  
9 327 The Office of Human Research Affairs at Albert Einstein College of Medicine approved this  
10  
11 328 study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the  
12  
13  
14 329 retrospective nature of our research.  
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16  
17 **330 Consent for publication**  
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19  
20 331 Non applicable.  
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23 **332 Availability of data and materials**  
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25  
26 333 The datasets used and/or analyzed during the current study are available from the corresponding  
27  
28 334 author on reasonable request.  
29  
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31  
32 **335 Competing interests**  
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34 336 No conflicts of interest exist.  
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36

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38

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3 345 **Author's Contributions**  
4

5 346 Design of the project: FC, XX, and UPJ.  
6

7 347 Underlying data verified by FC, XX, and UPJ.  
8

9 348 Acquisition, analysis, and interpretation of data: FC, XX, OM, RK, YAP, SRP, MJC, ADR, DS,  
10 349 and UPJ.  
11

12 350 Statistical analysis: FC and XX.  
13

14 351 Obtained funding: UPJ  
15

16 352 Manuscript writing: FC, XX, and UPJ.  
17

18 353 Critical revision of the manuscript for important intellectual content: FC, XX, OM, RK, YAP,  
19 354 SRP, MJC, ADR, DS, and UPJ.  
20

21 355 Supervision: UPJ  
22

23 356 All the Authors reviewed the work and approved the final version.  
24

25 357 FC and UPJ had full access to all the data in the study and take responsibility for the integrity of  
26 358 the data and the accuracy of the data analysis.  
27

28 359  
29

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31

32 361 Not applicable  
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**Table 1. Demographics, Past Medical History, and Clinical Characteristics of Admitted Patients**

	Spring (n=4495)		Summer (n=264)		Fall (n=377)		Winter (n=2254)	
	Sample	Value	Sample	Value	Sample	Value	Sample	Value
<b>30-Day hospital outcome</b>								
Still admitted - no (%)	4495	194 (4.3)	264	6 (2.3)	377	15 (4.0)	2254	103 (4.6)
Discharged alive - no (%)	4495	3177 (70.7)	264	229 (86.7)	377	336 (89.1)	2254	1893 (84.0)
Dead in the hospital - no (%)	4495	1124 (25.0)	264	29 (11.0)	377	26 (6.9)	2254	258 (11.4)
<b>Demographics</b>								
Age (IQR) - yr	4495	66 (55 - 77)	264	66 (50 - 76)	377	63 (50 - 73)	2254	67 (56 - 77)
Male sex - no (%)	4495	2377 (52.9)	264	138 (52.3)	377	198 (52.5)	2254	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	264	219 (83.0)	377	286 (75.9)	2254	1635 (74.2)
Body Mass Index (IQR) - kg/m <sup>2</sup>	4229	28.4 (24.6 - 33)	250	27.6 (22.5 - 32.7)	358	28.6 (25 - 34.1)	2194	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	264	81.7 (76.3 – 85.8)	377	87.6 (83.2 - 90.2)	2254	95.3 (91.9 – 101.8)
<b>Past Medical History</b>								
Hypertension - no (%)	4495	3370 (75)	264	197 (74.6)	377	254 (67.4)	2254	1713 (76)
Sleep apnea - no (%)	4495	521 (11.6)	264	28 (10.6)	377	47 (12.5)	2254	270 (12)
Hyperlipidemia - no (%)	4495	2609 (58)	264	153 (58)	377	199 (52.8)	2254	1380 (61.2)
Atrial fibrillation - no (%)	4495	449 (10)	264	30 (11.4)	377	35 (9.3)	2254	267 (11.8)

Chronic kidney disease - no (%)	4495	1406 (31.3)	264	70 (26.5)	377	85 (22.5)	2254	620 (27.5)
Heart failure - no (%)	4495	980 (21.8)	264	72 (27.3)	377	66 (17.5)	2254	519 (23)
Coronary artery disease - no (%)	4495	1316 (29.3)	264	95 (36)	377	108 (28.6)	2254	721 (32)
Asthma/COPD - no (%)	4495	1371 (30.5)	264	84 (31.8)	377	98 (26)	2254	753 (33.4)
Diabetes mellitus - no (%)	4495	2522 (56.1)	264	148 (56.1)	377	187 (49.6)	2254	1244 (55.2)
<b>Vitals at Presentation</b>								
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	264	98.4 (97.8 - 98.9)	372	98.8 (98.1 - 99.9)	2254	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	4469	131 (114 - 148)	264	132 (117 - 149)	375	131 (117 - 147)	2254	132 (117 - 148)
DBP (IQR) - mmHg	4465	75 (65 - 84)	263	77 (67 - 87)	374	74 (68 - 84)	2252	75 (67 - 84)
HR (IQR) – bpm	4467	98 (85 - 112)	264	92.5 (76.3 - 105)	372	94 (80 - 107)	2253	95 (82 - 107)
Oxygen saturation (IQR) - %	4463	95 (91 - 98)	264	98 (96 - 99)	372	96 (94 - 98)	2253	96 (92 - 98)
Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	264	18 (17 - 20)	372	18 (18 - 20)	2254	19 (18 - 22)
<b>Laboratory Markers</b>								
Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	261	12.4 (10.7 - 13.9)	370	13 (11.6 - 14.3)	2228	12.9 (11.5 - 14.2)
Platelet count (IQR) -k/ $\mu$ L	4372	188 (116 - 260)	261	228 (169 - 300)	372	200 (144 - 257)	2228	196 (143 - 259)
White blood cell count (IQR) - k/ $\mu$ L	4372	7.5 (5.6 - 10.6)	261	8 (5.8 - 11)	370	6.6 (5.1 - 8.9)	2228	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/ $\mu$ L	4420	1 (0.7 - 1.4)	263	1.2 (0.9 - 1.8)	374	1.1 (0.8 - 1.5)	2246	1 (0.7 - 1.4)
Sodium (IQR) – mEq/L	4414	137 (134 - 141)	263	138 (135 - 141)	377	137 (135 - 140)	2253	137 (134 - 140)



Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	262	4.2 (3.8 - 4.6)	377	4 (3.8 - 4.4)	2243	4.1 (3.8 - 4.5)
Chloride (IQR) – mEq/L	4394	98 (95 - 103)	263	103 (100 - 105)	377	101 (99 - 104)	2253	101 (98 - 104)
Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	263	24 (21 - 27)	377	25 (22 - 27)	2253	24 (21 - 27)
Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	263	1 (0.8 - 1.5)	377	1 (0.8 - 1.3)	2253	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	4414	134 (108 - 197)	263	121 (100 - 171)	377	122 (102 - 173)	2253	126 (104 - 184)
Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	245	26 (20 - 38)	354	31 (21 - 47)	2084	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	252	21 (14 - 32)	361	25 (16 - 41)	2171	26 (17 - 44)
Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	220	1.9 (1.4 - 2.7)	330	1.8 (1.3 - 2.5)	1913	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	160	254.5 (196 - 340)	285	300 (225 - 383)	1563	341 (254 - 468)
Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	209	97 (57 - 176)	313	116 (60 - 213)	1957	126 (67 - 282)
D-dimer (IQR) - µg/mL	2204	1.8 (0.9 - 3.9)	185	1.1 (0.5 - 2.2)	317	0.8 (0.5 - 1.6)	1907	1.2 (0.7 - 2.3)
Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	120	0.1 (0.1 - 0.4)	254	0.1 (0.1 - 0.2)	1252	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	0	NA	219	0.01 (0.01 - 0.03)	342	0.01 (0.01 - 0.02)	2106	0.01 (0.01 - 0.03)
Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	3	0.01 (0.01 - 0.01)	0	NA	0	NA
Interleukin-6 (IQR) – pg/mL	1056	33.6 (13.8 - 75.2)	87	11.7 (3 - 43.1)	186	11 (4.7 - 22.2)	710	10.8 (4.3 - 25.6)
Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	122	448 (370- 583)	224	540 (436 - 663)	1040	535.5 (434 - 652)

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Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	155	228 (90 - 562)	293	364 (166 - 785)	1637	510 (230 - 1094)
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COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

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**Table 2. Association with In-Hospital Mortality (Regression models with competing risks)**

Variable	Multivariable	
	HR (95% CI)	P-value
Age - yr	1.046 (1.04 - 1.051)	<0.001
Male sex - yes/no	1.352 (1.187 - 1.54)	<0.001
Body mass index - kg/m <sup>2</sup>	1.022 (1.012 - 1.032)	<0.001
Temperature - F	1.071 (1.036 - 1.108)	<0.001
SBP - mmHg	0.994 (0.991 - 0.997)	<0.001
DBP - mmHg	0.996 (0.991 - 1.001)	0.14
HR - bpm	1.003 (0.999 - 1.006)	0.11
Oxygen saturation - %	0.967 (0.961 - 0.972)	<0.001
Respiratory rate - bpm	1.027 (1.019 - 1.035)	<0.001
White blood cell count - k/ $\mu$ L	1.008 (1.001 - 1.016)	0.02
Glucose - mg/dL	1.001 (1 - 1.001)	0.001
Aspartate aminotransferase - U/L	1 (1 - 1.001)	0.21
Alanine aminotransferase - U/L	1 (0.999 - 1)	0.25
Lactic acid - mmol/L	1.071 (1.036 - 1.107)	<0.001
Platelet count - k/ $\mu$ L	0.999 (0.998 - 0.999)	<0.001
Potassium - mEq/L	1.096 (1.028 - 1.168)	0.0052
Bicarbonates - mEq/L	0.957 (0.944 - 0.971)	<0.001
Creatinine - mg/dL	1.023 (0.998 - 1.049)	0.069
HTN - yes/no	1.008 (0.851 - 1.194)	0.93
HLD - yes/no	1.196 (1.02 - 1.401)	0.027
CKD - yes/no	1.263 (1.09 - 1.462)	0.002
HF - yes/no	1.33 (1.146 - 1.543)	<0.001
COPD/Asthma - yes/no	0.948 (0.827 - 1.088)	0.45
DM - yes/no	0.946 (0.819 - 1.093)	0.45
CAD - yes/no	1.101 (0.955 - 1.271)	0.19
Statin use - %	0.577 (0.501 - 0.664)	<0.001
Bed occupancy - %	1.007 (1.002 - 1.013)	0.004

CAD = Coronary artery disease; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; DM = Diabetes mellitus; HLD = hyperlipidemia; HF = Heart failure; HR = Heart rate; HTN = Hypertension; SBP = Systolic blood pressure

## Figure Legends

### Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

### Figure 2. Cumulative Monthly Admission and Mortality

Cumulative monthly admissions (blue line, left axis) and mortality (orange line, right axis) over the year.

### Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

### Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.

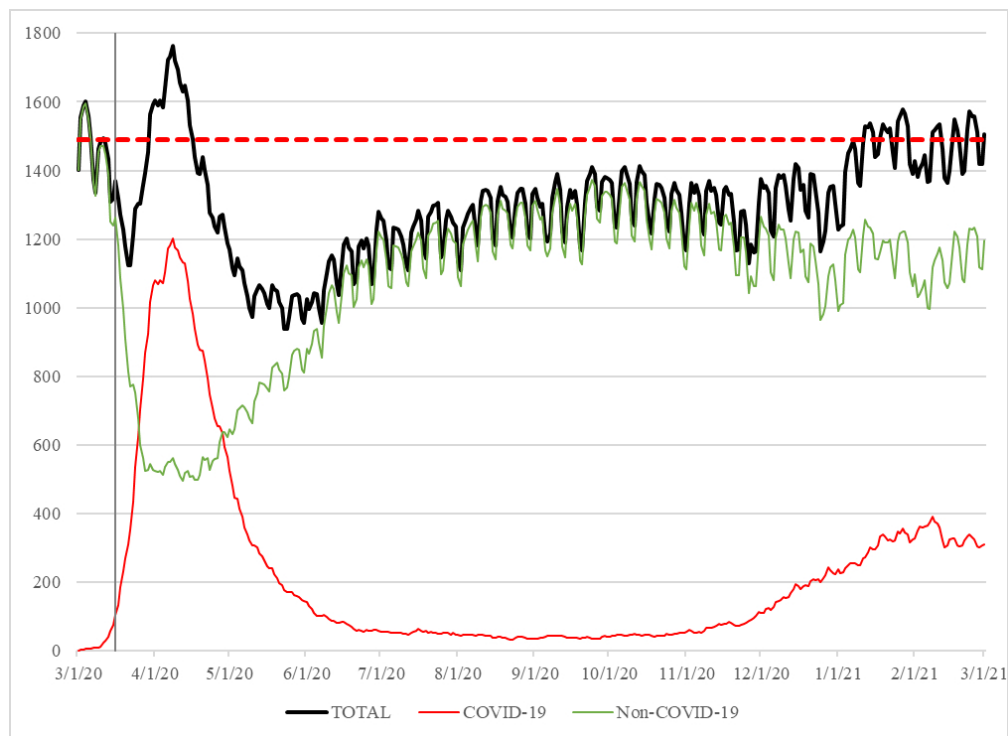


Figure 1

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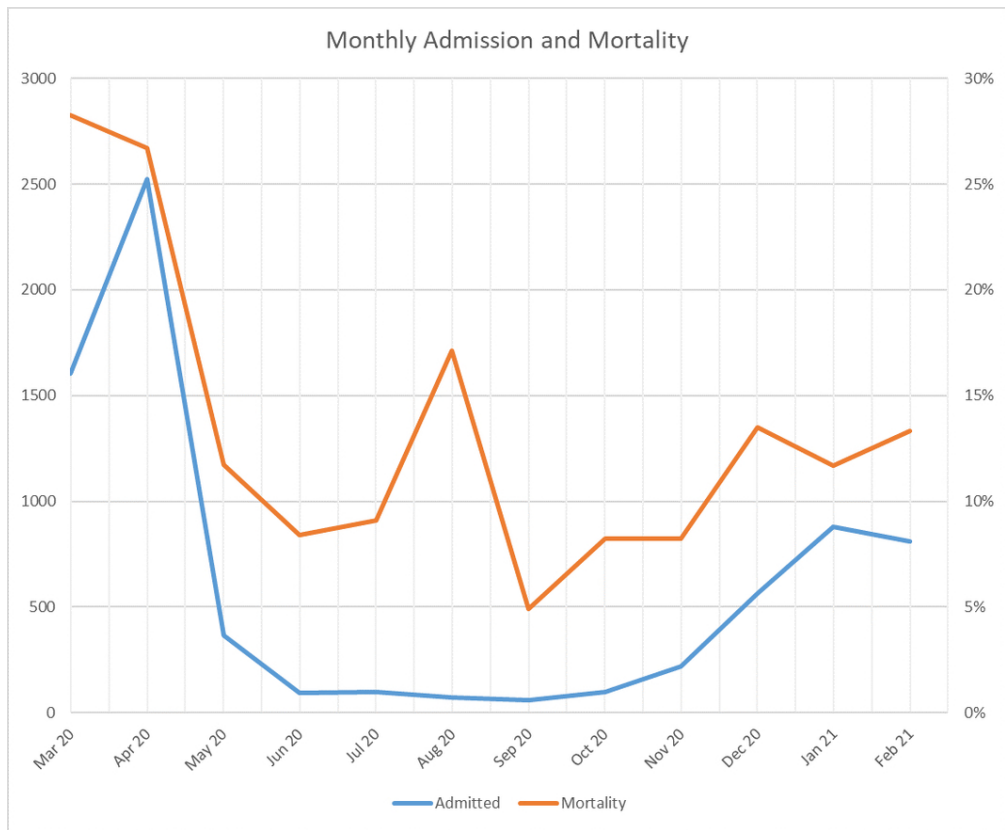


Figure 2

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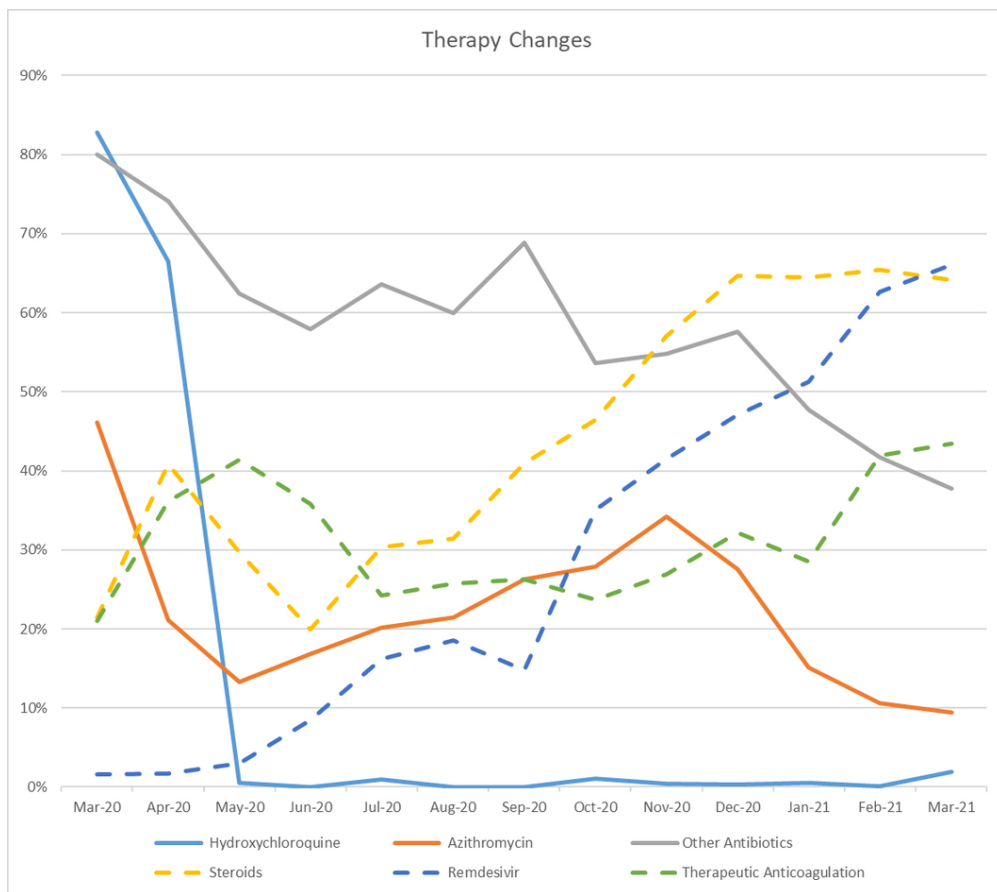


Figure 3

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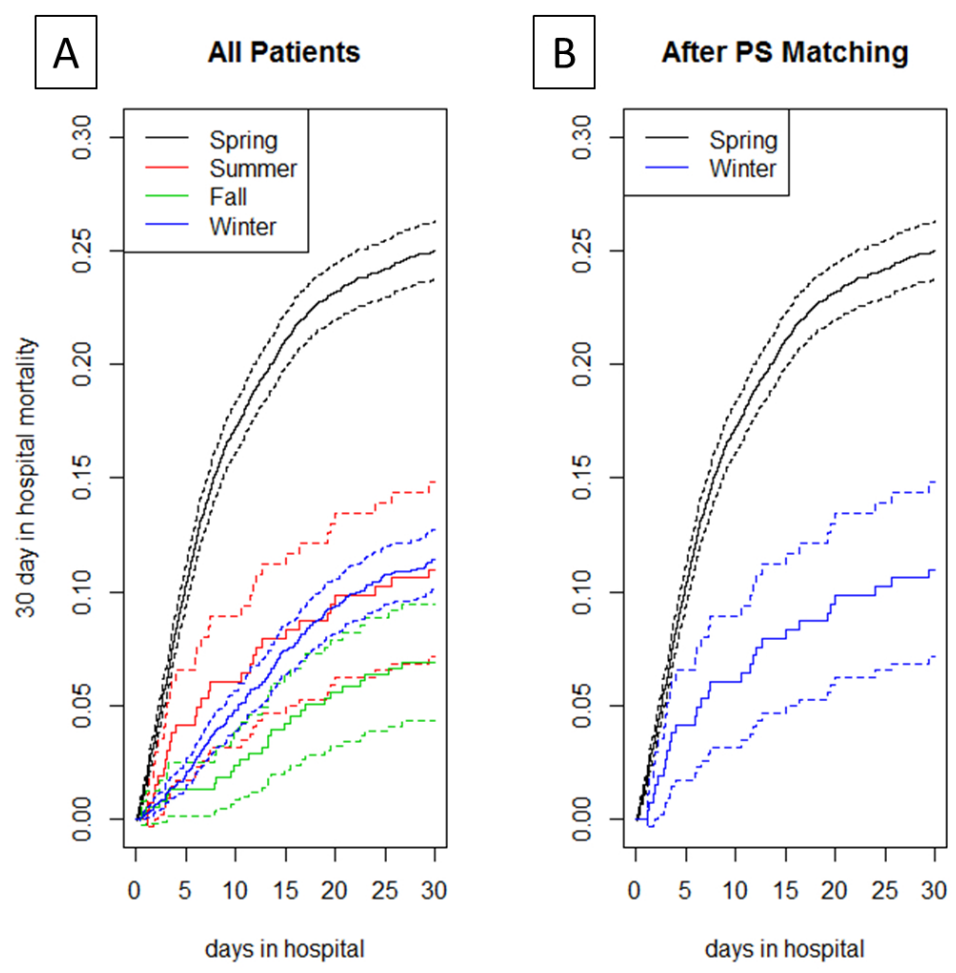


Figure 4

88x88mm (300 x 300 DPI)

**Supplemental Appendix**

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**Supplemental Table 1 - Comparison Survivors versus Non-survivors**

	Survivors (n=5953)		Non-survivors (n=1437)		p-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity – no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m <sup>2</sup>	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35
SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001
DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001

Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
<b>Laboratory Markers</b>					
Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
Platelet count (IQR) -k/ $\mu$ L	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
White blood cell count (IQR) - k/ $\mu$ L	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
Absolute lymphocyte count (IQR) - k/ $\mu$ L	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
Lactate dehydrogenase (IQR) - mmol/L	4017	384 $\pm$ 219	926	518 (371 - 706)	<0.001
Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777 $\pm$ 2657	<0.001
D-dimer (IQR) - $\mu$ g/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001
Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
Troponin I* (IQR) – ng/mL	2684	0.01 (0.01 – 0.02)	981	0.02 (0.01 - 0.08)	<0.001
Interleukin-6 (IQR) – pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
Fibrinogen (IQR) – mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001

Ferritin (IQR) – ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001
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COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

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## Supplemental Methods

### *Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients*

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 2**). These variables included: age, sex, BMI, vital signs at presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this model, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

**Supplemental Table 2 - Comparison Spring Vs Winter**

	Spring (n=4495)		Winter (n=2254)		P-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity – no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m <sup>2</sup>	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 – 107.6)	2254	95.3 (91.9 – 101.8)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001
SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) – bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001

1	Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
2						
3	Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
4						
5	<b>Laboratory Markers</b>					
6						
7						
8	Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
9						
10	Platelet count (IQR) -k/ $\mu$ L	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
11						
12	White blood cell count (IQR) - k/ $\mu$ L	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
13						
14	Absolute lymphocyte count (IQR) - k/ $\mu$ L	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
15						
16	Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
17						
18	Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
19						
20	Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
21						
22	Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
23						
24	Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
25						
26	Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
27						
28	Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
29						
30	Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
31						
32	Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
33						
34	Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
35						
36	Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
37						
38	D-dimer (IQR) - $\mu$ g/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001
39						
40	Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
41						
42	Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
43						
44	Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
45						
46	Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
47						
48	Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001
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Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001
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COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

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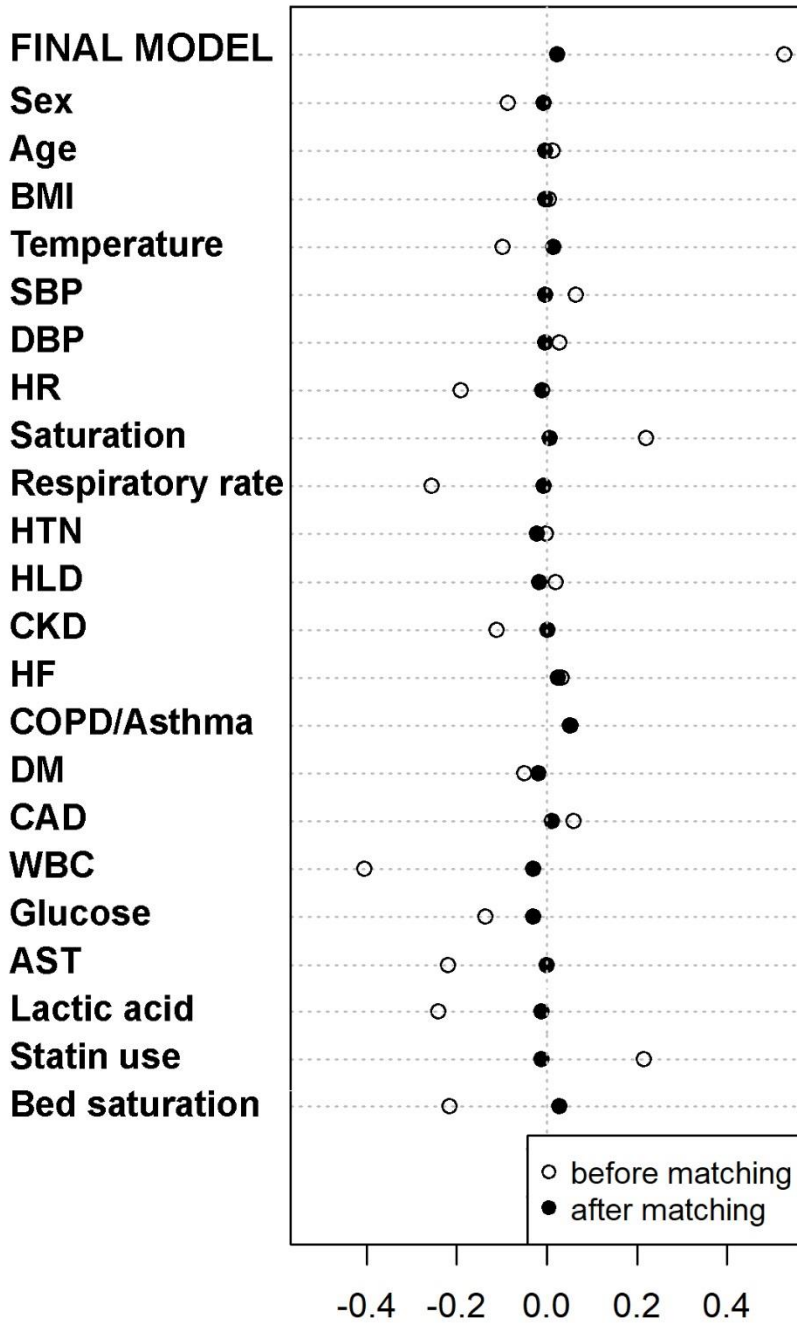
### Supplemental Table 3 - Therapies Administered during the Admission

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
<b>Hydroxychloroquine - no (%)</b>	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
<b>Azithromycin - no (%)</b>	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
<b>Other antibiotics - no (%)</b>	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
<b>Steroids - no (%)</b>	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
<b>Angiotensin-converting-enzyme Inhibitors - no (%)</b>	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
<b>Angiotensin II receptor blockers - no (%)</b>	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
<b>Statin - no (%)</b>	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
<b>Therapeutic anticoagulation - no (%)</b>	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
<b>Remdesivir* - no (%)</b>	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
<b>Lopinavir/Ritonavir – no (%)</b>	40 (0.9)	0 (0)	0 (0)	0 (0)
<b>Ivermectin – no (%)</b>	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

\* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.



Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12- 13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5-6  Supp
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	6-7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	6-9
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-9
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
5	<b>Discussion</b>			
6	Key results	18	Summarise key results with reference to study objectives	9
7	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
8	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
9	Generalisability	21	Discuss the generalisability (external validity) of the study results	14
10	<b>Other information</b>			
11	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Hospital Bed Occupancy Rate is An Independent Risk Factor for COVID-19 Inpatient Mortality: A Pandemic Epicenter Cohort Study

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Secondary Subject Heading:	Health policy, Infectious diseases, Public health
Keywords:	COVID-19, Public health < INFECTIOUS DISEASES, EPIDEMIOLOGY

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# Hospital Bed Occupancy Rate is An Independent Risk Factor for COVID-19 Inpatient Mortality: A Pandemic Epicenter Cohort Study

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Word count: 3,091

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1  
2  
3 **27 Abstract**  
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6 **28 Introduction:** COVID-19 first struck New York City in the spring of 2020 resulting in an  
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8 **29** unprecedented strain on our health care system triggering multiple changes in public health  
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11 **30** policy governing hospital operations as well as therapeutic approaches to COVID-19. We  
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13 **31** examined inpatient mortality at our center throughout the course of the pandemic.  
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16 **32 Methods:** Retrospective chart review of clinical characteristics, treatments, and outcome data of  
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18 **33** all patients admitted with COVID-19 from March 1<sup>st</sup>, 2020 to February 28<sup>th</sup>, 2021. Patients were  
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20  
21 **34** grouped into three-month quartiles. Hospital strain was assessed as percent of occupied beds  
22  
23 **35** based on a normal bed capacity of 1,491.  
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25

26 **36 Results:** Inpatient mortality decreased from 25.0% in spring to 10.8% over the course of the  
27  
28 **37** year. During this time, the use of Remdesivir, steroids, and anticoagulants increased; the use of  
29  
30 **38** hydroxychloroquine and other antibiotics decreased. Daily bed occupancy ranged from 62% to  
31  
32  
33 **39** 118% occupancy. In a multivariate model with all year's data controlling for demographics,  
34  
35 **40** comorbidities, and acuity of illness, percentage of bed occupancy was associated with increased  
36  
37 **41** 30-day in-hospital mortality of COVID-19 patients (0.7% mortality increase for each 1%  
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39 **42** increase in bed occupancy - HR 1.007, CI: 1.001, 1.013, p=0.004)  
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43 **43 Conclusion:** Inpatient mortality from COVID-19 was associated with bed occupancy. Early  
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45 **44** reduction in epicenter hospital bed occupancy to accommodate acutely ill and resource-intensive  
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47 **45** patients should be a critical component in the strategic planning for future pandemics.  
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3 47 **Strengths and limitations of this study**  
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- 6 48 • Large cohort study (7,390 COVID-19 patients).  
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8 49 • Longitudinal analysis over 1 year of management and hospital policy changes.  
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11 50 • Analysis of mortality changes after adjustment for different therapies and clinical  
12  
13 51 parameters.  
14  
15 52 • Identification of the association between level of hospital system stress and mortality,  
16  
17 with important public health ramifications.  
18 53  
19  
20 54 • Limitation: data on most recent variants are not included  
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## 56 INTRODUCTION

57 Coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health  
58 Organization on March 11<sup>th</sup>, 2020.<sup>1</sup> In the United States, after a cluster of cases reported from  
59 Washington state<sup>2</sup>, New York state quickly became the initial epicenter of this pandemic with  
60 over 1.27 million of cases till date and over 50,000 fatalities with the highest concentration in the  
61 Bronx and Queens boroughs of New York City.<sup>3</sup> Montefiore Einstein, with its three principal  
62 teaching hospitals and combined adult bed capacity of 1,491, is the primary health care provider  
63 for the large, nearly 1.5 million diverse population of the Bronx<sup>4</sup> and experienced a “first wave”  
64 of COVID-19 admissions in the spring of 2020<sup>3</sup>, followed by a significant reduction of cases  
65 until a second surge in hospitalizations was noted in the winter of 2020. Throughout the course  
66 of the year, multiple public health measures - including those adapting hospital operation to a  
67 disaster level pandemic, such as cancellation of all elective procedures and waiver of state  
68 specific licensing for health care providers - were put in place. In addition, the understanding of  
69 COVID-19 pathophysiology improved<sup>5,6</sup>, new treatments were developed<sup>7-10</sup>, parts of the  
70 general population<sup>11,12</sup> as well as hospital personnel developed antibodies after COVID-19  
71 illness<sup>13</sup>, and our hospital system adapted to and then recovered from crisis mode.<sup>14</sup> Here, we  
72 report outcomes of patients hospitalized with COVID-19 through one year since the first case,  
73 focusing on the differences observed between the spring and the winter surges.

## 75 METHODS:

### 76 Study Population

77 We retrospectively reviewed all adult patients admitted to Montefiore Medical Center with a real  
78 time reverse transcription polymerase chain reaction (RT-PCR) assay positive for COVID-19

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3 79 between March 1, 2020 and February 28, 2021. We divided this timeframe in four 3-month  
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5 80 seasons based on northern hemisphere calendar: spring (March 1, 2020 to May 31, 2020),  
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7 81 summer (June 1, 2020 to August 30, 2020), fall (September 1, 2020 to November 30, 2020), and  
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9 82 winter (December 1, 2020 to February 28, 2021).  
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### 14 84 **Data Collection**

15  
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17 85 Medical data including demographic, clinical, and laboratory variables were extracted from the  
18  
19 86 electronic medical record system. The primary outcome was 30-day in-hospital mortality.  
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### 24 88 **Statistical Analysis**

25  
26 89 Continuous variables are displayed as mean  $\pm$  standard deviation or median [25-75%  
27  
28 90 interquartile range] and compared with the Student's t-test, or Wilcoxon ranks-sum, as  
29  
30 91 appropriate. Categorical data are presented as percent and compared by the chi-squared test. We  
31  
32 92 estimated the cumulative incidence of the primary endpoint in-hospital mortality for each season,  
33  
34 93 treating hospital discharge as a competing event.<sup>15</sup> To avoid any bias due to differential follow-  
35  
36 94 up length, we censored the follow-up time at 30 days after the admission.  
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40 95 A multivariable competing risk proportional hazard models was used to estimate the sub-  
41  
42 96 distribution hazard ratios<sup>16 17</sup> for time to in-hospital death. The covariates in the multivariable  
43  
44 97 analyses included factors present in > 90% of our dataset, known to be associated with in-  
45  
46 98 hospital COVID-19 mortality based on prior literature<sup>6 18 19</sup>, or with a univariate association with  
47  
48 99 in-hospital mortality ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between  
49  
50 100 survivors and non survivors (**Supplemental Table 1**). These variables included: age, sex, body  
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52 101 mass index (BMI), vital signs at presentation (temperature, systolic and diastolic blood pressure,  
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3 102 heart rate, respiratory rate, pulse oxygen saturation), platelet count, white cell count, potassium,  
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5 103 bicarbonate, creatinine, glucose, alanine transaminase, aspartate transaminase, history of  
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8 104 hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease,  
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10 105 asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Additionally,  
11  
12 106 lactic acid level and percent of hospital bed saturation were forced into the model as marker of  
13  
14  
15 107 illness severity and level of hospital stress, respectively.  
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20 109 Then we focused on examining the difference in in-hospital death between patients admitted in  
21  
22 110 the spring and in the winter, as they represented the two largest and most temporal distant waves  
23  
24 111 of the COVID-19 pandemic occurring before and after public health polices, specific therapeutic  
25  
26 112 approaches and hospital management changes had been implemented. Selection method for  
27  
28 113 covariates is presented in the **Supplemental Material** and **Supplemental Table 2**.

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30  
31 114 The proportionality assumption was examined<sup>20</sup> and no violation was identified. A two-sided  
32  
33 115  $p < 0.05$  was considered statistically significant.  
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36 116

### 37 38 117 **Propensity Score Analysis**

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40  
41 118 To fully control the potential differences in patient population and hospital stress between spring  
42  
43 119 and winter COVID-19 patients, we also used propensity score (PS) matching to compare the 30-  
44  
45 120 day in-hospital mortality between spring and winter admissions. The same covariates used for  
46  
47 121 the multivariable competing risk regression were used for PS matching. PS matching was carried  
48  
49 122 out through a 1:1 greedy matching algorithm, with a caliper width of 0.1 SD. We then stratified  
50  
51 123 on matched pair in the competing risk regression model.<sup>21 22</sup> Because one-to-one matching led to  
52  
53 124 a reduction in sample size, we used this analysis as a sensitivity analysis.  
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3 125 All statistical analyses was performed with SPSS (IBM Corp, ver. 25, Armonk, NY) and the R  
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5 126 packages cmprsk and crrSC (R Foundation for Statistical Computing, ver 3.5)  
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## 9 10 128 **Patient and Public Involvement**

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12 129 Given the retrospective nature of our analysis, it was not appropriate or possible to involve  
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14 130 patients or the public in the design, or conduct, or reporting, or dissemination plans of our  
15  
16 131 research.  
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19 132

## 20 21 133 **RESULTS**

22  
23 134 7,390 COVID-19 positive adult patients were admitted between March 1, 2020 and February 28,  
24  
25 135 2021 (**Figure 1**). 4,495 patients were admitted during the spring, 264 during the summer, 377  
26  
27 136 during the fall, and 2,254 during the winter.  
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31 137 On April 8, 2020, peak of the spring season, the total numbers of simultaneously adult patients  
32  
33 138 admitted to our hospital (including those admitted to emergency adult wards at our children's  
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35 139 hospital<sup>23</sup>) was 1,762 (118% of nominal bed capacity); 1,201 of them (68.2%) were COVID-19  
36  
37 140 patients. On February 8, 2021, peak of winter season, 1,512 patients (101% of nominal bed  
38  
39 141 capacity) were admitted to our hospital and 393 of them (26.0%) were COVID-19 patients.  
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41

42 142 (**Figure 1**). Following cancellation of elective procedures, bed occupancy decreased to 70% by  
43  
44 143 the end of the spring season and remained at 90% until the beginning of the winter season, when  
45  
46 144 the second wave occurred in December 2020. Unadjusted mortality for patient admitted at the  
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48 145 beginning of spring, end of spring, beginning of winter, and end of winter was 28%, 8%, 14%,  
49  
50 146 and 13%, respectively (**Figure 2**).  
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## 148 **Patient Population**

149 Demographics, past medical history, vital signs at arrivals are presented in **Table 1**. Initial  
150 laboratory blood tests are presented in **Supplemental Table 3**. Overall, median age was 66 (55 –  
151 77) years, 3,835 (51.9%) patients were male, 5,519 (74.2%) were of Black race and/or Hispanic  
152 ethnicity. Median age ranged from 63 years (fall) to 67 years (spring). Sex distribution was  
153 similar throughout the year. Summer and fall patients had the lowest and the highest BMI: 26.7  
154 and 28.6 kg/m<sup>2</sup>, respectively.

## 156 **Pharmacotherapy**

157 Changes in pharmacological approach is presented in **Supplemental Table 4** and **Figure 3**.  
158 Spring patients were more likely to receive hydroxychloroquine, azithromycin and other  
159 antibiotics. The use of Remdesivir substantially increased throughout the year (from less than 2%  
160 during spring to almost 70% by the end of the winter). Steroids prescription (from 33% during  
161 spring to almost 70% in February 2021), therapeutic anticoagulation therapy, as well as use of  
162 statins, angiotensin converting inhibitors (ACE-I), or angiotensin receptor blockers (ARBs) also  
163 increased.

## 165 **Death, Intubation, and Length of Stay**

166 Over the course of a year, 1,437 (19.4%) died while hospitalized. Patients who died were older,  
167 had more comorbidities, and were more acutely ill consistent within prior reports on risk factors  
168 for death in COVID-19<sup>5 6</sup> (**Supplemental Table 1**). Average unadjusted monthly mortality is  
169 presented in **Figure 2**. 30-day in-hospital mortality (**Figure 4A**) was 25.0% for the spring  
170 patients, 11.0% for summer patients, 6.9% for fall patients, and 11.4% for winter patients

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3 171 ( $p < 0.001$ ). On average, spring patients died 6.4 (3.2 – 12.9) days after the arrival to the  
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5 172 emergency department, summer patients 7.2 (3.0 – 15.7) days after the arrival, fall patients 13.4  
6  
7 173 (8.7 – 21.6) days after arrival, and winter patients 13.3 (6.8 – 20.7) days after the arrival  
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9  
10 174 ( $p < 0.001$ ). Frequency of invasive ventilatory support was higher during the spring with 892  
11  
12 175 patients (19.4%) intubated, versus 27 (10.2%) in the summer, 36 (9.5%) during fall, and 268  
13  
14 176 (11.9%) in the winter,  $p < 0.001$ . Median time from arrival-to-intubation was 0.7 (0.1 - 4.1) days  
15  
16 177 for spring patients, 0.6 (0.1 - 8.1) days for summer patients, 2.2 (0.1 – 7.3) days for fall patients,  
17  
18 178 and 2.8 (0.3 – 7.0) days for winter patients,  $p < 0.001$ . Median length of stay was 6.1 (3.5 – 11.1)  
19  
20 179 days during spring, 5.1 (2.7 – 10.1) days during summer, 5.0 (3.0 – 10.1) days during fall, and  
21  
22 180 6.3 (3.8 – 12.0) days during winter,  $p < 0.001$ .

181

## 182 **Bed Saturation and Mortality**

183 We defined bed saturation the percentage of bed occupancy calculated from the ratio between the  
184 number of admitted patients over the nominal bed capacity of our institution (1,491).

185 In the multivariable competing risk proportional hazard model of the entire cohort, percent of  
186 bed occupancy was associated with increased 30-day in-hospital mortality (HR 1.007, CI: 1.001,  
187 1.013,  $p = 0.004$ ); i.e mortality increase by 0.7 % for each 1% increase of bed occupancy.

188 Consistent results were observed per level increase in bed occupancy quartile, (HR 1.086 [1.026  
189 -1.148], P-value for linear trend = 0.004). Results of the competing risk regression analysis are  
190 presented in the **Table 2**.

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## 192 **Spring vs Winter Mortality Comparison and Propensity Matched Analysis**

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3 193 In the multivariable competing risk proportional hazard model comparing spring and winter  
4  
5 194 season, 30-day in-hospital mortality was lower in winter (HR 0.520, CI 0.448-0.604,  $p < 0.001$ )  
6  
7  
8 195 when compared to spring. After PS caliper matching, there were 1,722 matched pairs. Spring and  
9  
10 196 winter patients had similar distribution of PS (**Supplemental Figure 1**) and standardized average  
11  
12 197 difference among covariates was greatly reduced. PS analysis showed a significant reduction of  
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14  
15 198 in-hospital mortality during winter (HR 0.580 CI: 0.507-0.663,  $p < 0.001$ ) confirming what we  
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17 199 observed in the multivariable adjusted analysis (**Figure 4B**).  
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## 201 **DISCUSSION**

202 We examined inpatient mortality from COVID-19 over the course of a one-year pandemic at our  
203 hospital system in New York City. Our principal findings are as follows: First, we observed a  
204 substantial reduction of in-hospital mortality coinciding with multiple pandemic related public  
205 health measures focusing on hospital resource management – and preceding comprehensive  
206 changes in pharmacotherapy - towards the end of the first surge. Second, we describe - for the  
207 first time - hospital bed occupancy as an independent risk factor for inpatient mortality from  
208 COVID-19.  
209

### 210 **Public Health Measures in Response to COVID-19**

211 After declaring a state of disaster emergency (March 7, 2020), New York State introduced  
212 different measures to limit the spread of the disease, including public schools closure (March 16,  
213 2020), limitation of indoor dining (March 17, 2020), stay-home order for non-essential workers  
214 (March 22, 2020), mandatory face coverings in public (April 15, 2020), and night subway  
215 closure (April 30, 2020)<sup>24</sup>. Despite these measures to limit the diffusion of the disease and a

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3 216 generalized reduction of movements around New York City (as evidenced by a more than 90%  
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5 217 reduction of subway ridership compared to 2019)<sup>25</sup>, more than 30% of Bronx residents were  
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7 218 found to have positive antibodies (and thus possibly temporary immunity) against SARS-CoV-2  
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9 219 in August 2020.<sup>26</sup>  
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11  
12 220 Specifically relevant to hospital operations, executive order no. 202.5 (March 16, 2020)<sup>27</sup>  
13  
14 221 allowed healthcare providers not licensed or registered in New York State to temporarily work in  
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16 222 the State, and executive order no. 202.10 (March 22, 2020)<sup>27</sup> suspended elective operations.  
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18 223 These executive orders were associated with a dramatic drop in non-COVID-19 admissions at  
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20 224 our institution beginning March 16, 2020. (**Figure 1**). On March 26, 2020 New York State  
21  
22 225 Governor Cuomo additionally mandated all hospitals to increase their bed capacity by 50% to  
23  
24 226 accommodate the surge of COVID-19 patients.<sup>27</sup> Despite this order, the actual bed occupancy at  
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26 227 our institution (while accommodating all COVID-19 patients presenting to our hospitals)  
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28 228 remained below the usual operating capacity until December 2020.  
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31 229 Notably, COVID-19 mortality remained stable throughout the summer and fall 2020 with low  
32  
33 230 case counts and increased utilization of steroids, anticoagulation, and remdesivir. Although  
34  
35 231 randomized controlled trials have shown morbidity benefits with the use of remdesivir<sup>7</sup> and  
36  
37 232 mortality reduction with steroids<sup>8</sup>, the magnitude of these effects cannot explain the more than  
38  
39 233 50% reduction in mortality we observed. Furthermore, pharmacotherapy, with the exception of  
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41 234 hydroxychloroquine elimination, did not materially change within the spring season, by the end  
42  
43 235 of which mortality was already decreased. Steroid, remdesivir, and therapeutic anticoagulation  
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45 236 were used in 10-20% of patients by May 2020, but they reached 30-70% only in the winter  
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47 237 season. Despite that, unadjusted mortality began to increase again in December 2020 during the  
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238 second wave. Of note, bed occupancy also increased at that time and proved to be an  
239 independent risk factor for COVID-19 mortality in our cohort of nearly 8,000 patients.

240

### 241 **Change in Therapeutic Approach**

242 The initial widespread (>2/3 of first spring patients) use of hydroxychloroquine, an agent  
243 eventually proven to be ineffective<sup>28</sup> to treat COVID-19, probably represents the most obvious  
244 pandemic-associated deviation from the usual multiphase clinical trial standards of therapeutic  
245 paradigm development. Only 8 of 2,254 patients received hydroxychloroquine during the winter  
246 wave. Similarly, we observed a reduction in the use of azithromycin and other antibiotics, the  
247 latter possibly reflecting a more careful assessment of the need to treat superimposed bacterial  
248 infections during the second wave. Steroid therapy<sup>8 29</sup> and therapeutic anticoagulation<sup>9</sup> were  
249 implemented in the majority of patients during the winter after the knowledge on the likely  
250 disease modulating inflammatory properties and pro-thrombotic effect of COVID-19 had been  
251 recognized<sup>30</sup> and, in the case of steroids, a therapeutic effect had been proven<sup>8</sup>. Remdesivir, an  
252 inhibitor of the viral RNA-dependent RNA polymerase that showed shortening of recovery time  
253 in hospitalized patients with COVID-19<sup>7</sup>, received emergency FDA approval on October  
254 22<sup>nd</sup>, 2020<sup>31</sup> and was administered to almost half of the admitted patients during the winter. If  
255 initial concerns of possible interactions between ACE-I or ARBs and SARS-CoV-2<sup>32</sup> led to a  
256 possible underutilization or discontinuation of these drugs during the spring, we observed a  
257 significant increase in their use during the following months, after no increased risks were  
258 reported.<sup>33 34</sup>

259 Similarly, after several reports showed a possible protective effect associated with the use of  
260 statins<sup>35 36</sup>, their utilization markedly increased during the winter.

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3 261 Lastly, after the spring wave provided anecdotal evidence for early proning in COVID-19  
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5 262 pneumonia, an approach strongly favoring noninvasive ventilation and avoiding intubation was  
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7 263 developed to address respiratory distress in COVID-19; more data about such an approach has  
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9  
10 264 since accumulated.<sup>10 37</sup> The cumulative effect of these therapeutic changes, in combination with  
11  
12 265 a better preparedness to respond to a pandemic, can be estimate from the different mortality  
13  
14 266 between the first surge (spring) and the second surge (winter). After matching the two groups for  
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16 267 demographic and clinical variables, as well as for elements indicative of hospital distress (bed  
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18 268 occupancy), a significant reduction of mortality was observed during the winter trimester.  
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### 24 270 **Change in Hospital Stress Load**

25  
26 271 At the peak of the pandemic, the hospital saturation reached the 118% of the nominal bed  
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28 272 capacity and COVID-19 patients accounted for 68.2% of all admitted patients. This increase in  
29  
30 273 acutely ill patients created significant excess demand on the rest of the hospital infrastructure  
31  
32 274 best characterized by the surge in the need for intensive care unit (ICU) beds and transformation  
33  
34 275 of other hospital areas to ICUs.<sup>14 23</sup> Despite increased patient load, the number of standard ICU  
35  
36 276 beds, as well as laboratories, diagnostic equipment, and available personnel, remained the same  
37  
38 277 as before the pandemic. This unmatched patient overload resulted in a 0.7 % mortality increase  
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40 278 for each 1% increment in hospital bed saturation. In light of these results, strategies to minimize  
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42 279 the bed occupancy for non-Covid-19 patients or non-life-saving admission should be adopted to  
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44 280 diverge resources to improve the outcome of admitted Covid-19 patients.  
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### 51 282 **Limitations**

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3 283 Our study has the shortcomings of a retrospective investigation, but there are some very specific  
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5 284 aspects limiting the interpretation of our results. First, it is difficult to assess the true effects of  
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8 285 pharmacotherapy given the dynamic changes in indications, doses, and usage that happened over  
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10 286 the course of the year. Regardless, we believe the propensity-matched comparison between the  
11  
12 287 spring and the winter waves provides compelling evidence for the validity of our principal  
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14 288 observation of inpatient COVID-19 mortality reduction disproportionate to advances in  
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16 289 pharmacotherapy. We chose total bed occupancy as a metric for hospital stress assuming that  
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18 290 other resources per bed remained static. Notably, the ratio of COVID-19 to non-COVID-19  
19  
20 291 patients, ICU bed saturation, and staff shortages are unaccounted for in this model. Regrettably,  
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22 292 an in-depth analysis of these metrics is beyond our ability in this retrospective pandemic analysis  
23  
24 293 with disaster elements. Additionally, a significant number of patients received ICU-level-of-care  
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26 294 interventions (mechanical ventilatory support, dialysis, vasopressors titration) on regular floors;  
27  
28 295 therefore, the concept of ICU bed saturation might have been not truly representative of the  
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30 296 burden.  
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35 297 However, we feel our data is sufficiently strong to support the notion that bed capacity expansion  
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37 298 alone is not the answer. Rather, a smaller number of beds with higher staffing accomplished by  
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39 299 drastic reductions in all non-emergent procedures and activities is likely a better approach.  
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41  
42 300 Although offering fewer beds in pandemic situation appears initially quite counterintuitive, in  
43  
44 301 practice we observed that mortality began to decrease once beds and resources were allocated  
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46 302 specifically to COVID-19 patients by executive orders 202.5 and 202.10; and most importantly  
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48 303 that bed occupancy never exceeded 100% once hospital operations focused on the COVID-19  
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50 304 pandemic only. It is conceivable that an uptrend in mortality observed late in the pandemic with  
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52 305 established treatment paradigms could be due to new viral strains or a sicker patient population.  
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3 306 Although we are unable to provide detailed strain analysis for our study population, a meaningful  
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5 307 numbers of new (and possibly more virulent) strains were not yet observed in in the Bronx,  
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7 308 where our study was conducted.<sup>38</sup> The small sample size of patients in summer and fall does not  
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9  
10 309 allow meaningful propensity matched comparisons, and when comparing summer, fall, and  
11  
12 310 winter populations, there do not appear to be clinically meaningful differences. Lastly, single-  
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14 311 patient data on vaccination status were not available. At the conclusion of the study, only 13.8%  
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16 312 of the population of New York State received at least one dose and 7.4% received two doses<sup>39</sup>.  
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18 313 Given the heterogeneous distribution of vaccination within the state (and the city of New York),  
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20 314 it is impossible to meaningfully account for these parameters.  
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## 26 316 **CONCLUSIONS**

27  
28 317 Inpatient mortality from COVID-19 decreased to a degree disproportionate to advances in  
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30 318 disease specific therapeutics. Increased bed occupancy was associated to a higher in-hospital  
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32 319 mortality. Implementation of non-pharmacological approaches and other seasonal variations  
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34 320 might also had a role in the mortality reduction.. Early reduction in epicenter hospital bed  
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36 321 occupancy to accommodate acutely ill and resource-intensive patients should be a critical  
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38 322 component in the strategic planning for future pandemics.  
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3 325 **DECLARATIONS**  
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6 326 **Ethics approval and consent to participate**  
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9 327 The Office of Human Research Affairs at Albert Einstein College of Medicine approved this  
10  
11 328 study (# 2020-11308). Patient consent and HIPAA forms were waived by our IRB due to the  
12  
13  
14 329 retrospective nature of our research.  
15

16  
17 330 **Consent for publication**  
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19  
20 331 Non applicable.  
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23 332 **Availability of data and materials**  
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25  
26 333 The datasets used and/or analyzed during the current study are available from the corresponding  
27  
28 334 author on reasonable request.  
29  
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31  
32 335 **Competing interests**  
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34 336 No conflicts of interest exist.  
35  
36

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38

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46  
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48  
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3 345 **Author's Contributions**  
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5 346 Design of the project: FC, XX, and UPJ.  
6

7 347 Underlying data verified by FC, XX, and UPJ.  
8

9 348 Acquisition, analysis, and interpretation of data: FC, XX, OS, RK, YAP, SRP, MJG, ADR, DS,  
10 349 and UPJ.  
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12 350 Statistical analysis: FC and XX.  
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14 351 Obtained funding: UPJ  
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16 352 Manuscript writing: FC, XX, and UPJ.  
17

18 353 Critical revision of the manuscript for important intellectual content: FC, XX, OS, RK, YAP,  
19 354 SRP, MJG, ADR, DS, and UPJ.  
20

21 355 Supervision: UPJ  
22

23 356 All the Authors reviewed the work and approved the final version.  
24

25 357 FC and UPJ had full access to all the data in the study and take responsibility for the integrity of  
26 358 the data and the accuracy of the data analysis.  
27

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**Table 1. Demographics, Past Medical History, and Vital Signs of Admitted Patients**

	Spring (n=4495)	Summer (n=264)	Fall (n=377)	Winter (n=2254)
<b>30-Day hospital outcome</b>				
Still admitted - no (%)	194 (4.3)	6 (2.3)	15 (4.0)	103 (4.6)
Discharged alive - no (%)	3177 (70.7)	229 (86.7)	336 (89.1)	1893 (84.0)
Dead in the hospital - no (%)	1124 (25.0)	29 (11.0)	26 (6.9)	258 (11.4)
<b>Demographics</b>				
Age (IQR) – yr	66 (55 - 77)	66 (50 - 76)	63 (50 - 73)	67 (56 - 77)
Male sex - no (%)	2377 (52.9)	138 (52.3)	198 (52.5)	1122 (49.8)
Black race and / or Hispanic ethnicity – no (%)	3345 (74.4)	219 (83.0)	286 (75.9)	1635 (74.2)
Body Mass Index (IQR) - kg/m <sup>2</sup>	28.4 (24.6 - 33)	27.6 (22.5 - 32.7)	28.6 (25 - 34.1)	28.2 (24.4 - 33.1)
Hospital bed saturation (IQR) - %	97.4 (86.5 – 107.6)	81.7 (76.3 – 85.8)	87.6 (83.2 - 90.2)	95.3 (91.9 – 101.8)
<b>Past Medical History</b>				
Hypertension - no (%)	3370 (75)	197 (74.6)	254 (67.4)	1713 (76)
Sleep apnea - no (%)	521 (11.6)	28 (10.6)	47 (12.5)	270 (12)
Hyperlipidemia - no (%)	2609 (58)	153 (58)	199 (52.8)	1380 (61.2)
Atrial fibrillation - no (%)	449 (10)	30 (11.4)	35 (9.3)	267 (11.8)
Chronic kidney disease - no (%)	1406 (31.3)	70 (26.5)	85 (22.5)	620 (27.5)
Heart failure - no (%)	980 (21.8)	72 (27.3)	66 (17.5)	519 (23)
Coronary artery disease - no (%)	1316 (29.3)	95 (36)	108 (28.6)	721 (32)
Asthma/COPD - no (%)	1371 (30.5)	84 (31.8)	98 (26)	753 (33.4)
Diabetes mellitus - no (%)	2522 (56.1)	148 (56.1)	187 (49.6)	1244 (55.2)
<b>Vitals at Presentation</b>				
Temperature (IQR) - F	98.9 (98.2 - 100)	98.4 (97.8 - 98.9)	98.8 (98.1 - 99.9)	98.7 (98.1 - 99.8)
SBP (IQR) - mmHg	131 (114 - 148)	132 (117 - 149)	131 (117 - 147)	132 (117 - 148)
DBP (IQR) - mmHg	75 (65 - 84)	77 (67 - 87)	74 (68 - 84)	75 (67 - 84)
HR (IQR) – bpm	98 (85 - 112)	92.5 (76.3 - 105)	94 (80 - 107)	95 (82 - 107)
Oxygen saturation (IQR) - %	95 (91 - 98)	98 (96 - 99)	96 (94 - 98)	96 (92 - 98)
Respiratory Rate (IQR) - bpm	20 (18 - 22)	18 (17 - 20)	18 (18 - 20)	19 (18 - 22)

COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure.

**Table 2. Association with In-Hospital Mortality (Regression models with competing risks)**

Variable	Multivariable	
	HR (95% CI)	P-value
Age - yr	1.046 (1.04 - 1.051)	<0.001
Male sex - yes/no	1.352 (1.187 - 1.54)	<0.001
Body mass index - kg/m <sup>2</sup>	1.022 (1.012 - 1.032)	<0.001
Temperature - F	1.071 (1.036 - 1.108)	<0.001
SBP - mmHg	0.994 (0.991 - 0.997)	<0.001
DBP - mmHg	0.996 (0.991 - 1.001)	0.14
HR - bpm	1.003 (0.999 - 1.006)	0.11
Oxygen saturation - %	0.967 (0.961 - 0.972)	<0.001
Respiratory rate - bpm	1.027 (1.019 - 1.035)	<0.001
White blood cell count - k/ $\mu$ L	1.008 (1.001 - 1.016)	0.02
Glucose - mg/dL	1.001 (1 - 1.001)	0.001
Aspartate aminotransferase - U/L	1 (1 - 1.001)	0.21
Alanine aminotransferase - U/L	1 (0.999 - 1)	0.25
Lactic acid - mmol/L	1.071 (1.036 - 1.107)	<0.001
Platelet count - k/ $\mu$ L	0.999 (0.998 - 0.999)	<0.001
Potassium - mEq/L	1.096 (1.028 - 1.168)	0.0052
Bicarbonates - mEq/L	0.957 (0.944 - 0.971)	<0.001
Creatinine - mg/dL	1.023 (0.998 - 1.049)	0.069
HTN - yes/no	1.008 (0.851 - 1.194)	0.93
HLD - yes/no	1.196 (1.02 - 1.401)	0.027
CKD - yes/no	1.263 (1.09 - 1.462)	0.002
HF - yes/no	1.33 (1.146 - 1.543)	<0.001
COPD/Asthma - yes/no	0.948 (0.827 - 1.088)	0.45
DM - yes/no	0.946 (0.819 - 1.093)	0.45
CAD - yes/no	1.101 (0.955 - 1.271)	0.19
Statin use - %	0.577 (0.501 - 0.664)	<0.001
Bed occupancy - %	1.007 (1.001 - 1.013)	0.004

CAD = Coronary artery disease; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; DM = Diabetes mellitus; HLD = hyperlipidemia; HF = Heart failure; HR = Heart rate; HTN = Hypertension; SBP = Systolic blood pressure

## Figure Legends

### Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

### Figure 2. Cumulative Monthly Admissions and Mortality

Cumulative monthly admissions (black line, left axis) and mortality (dotted red line, right axis) over the year.

### Figure 3. Change in Therapies

Percent of patients receiving specific therapies over the year.

### Figure 4. Cumulative Incidences

30-day in-hospital mortality by seasons.

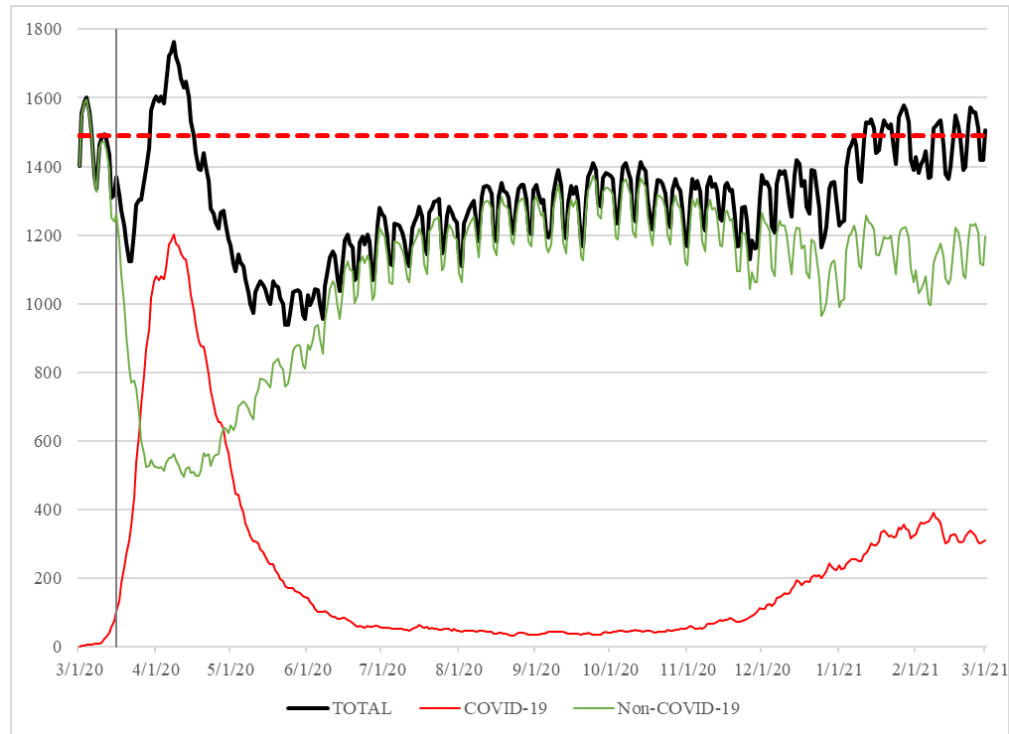


Figure 1. Simultaneously Admitted Patients

This graph includes the hospitalized patients and the admitted patients in the emergency department waiting for a bed. A precipitous decline of non-COVID-19 admissions begins on March 16, 2020 (vertical gray line) coinciding with gubernatorial health care associated directives in the State of New York. The dotted red line indicates the nominal bed capacity of our institution (1,491 beds).

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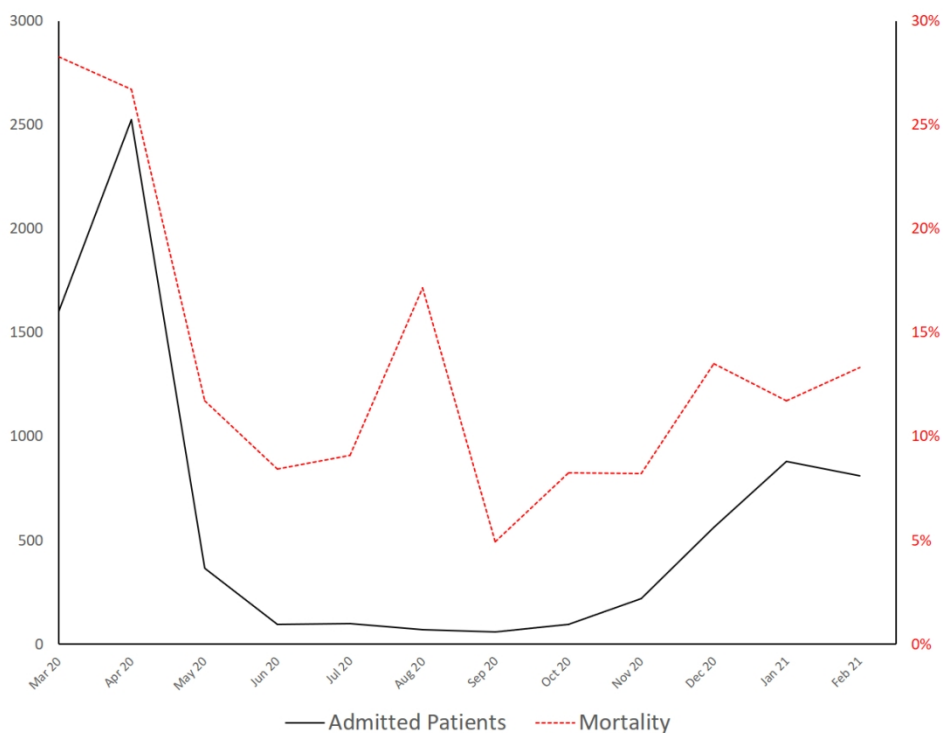


Figure 2. Cumulative Monthly Admissions and Mortality  
 Cumulative monthly admissions (black line, left axis) and mortality (dotted red line, right axis) over the year.

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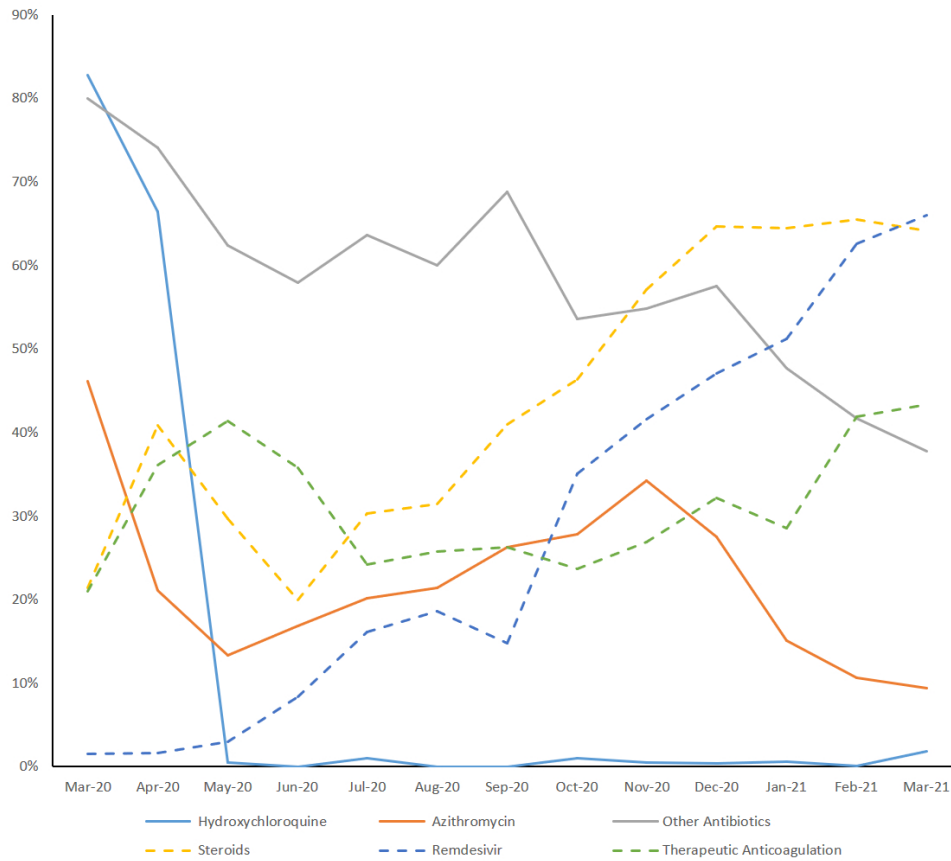


Figure 3. Change in Therapies  
Percent of patients receiving specific therapies over the year.

97x85mm (300 x 300 DPI)

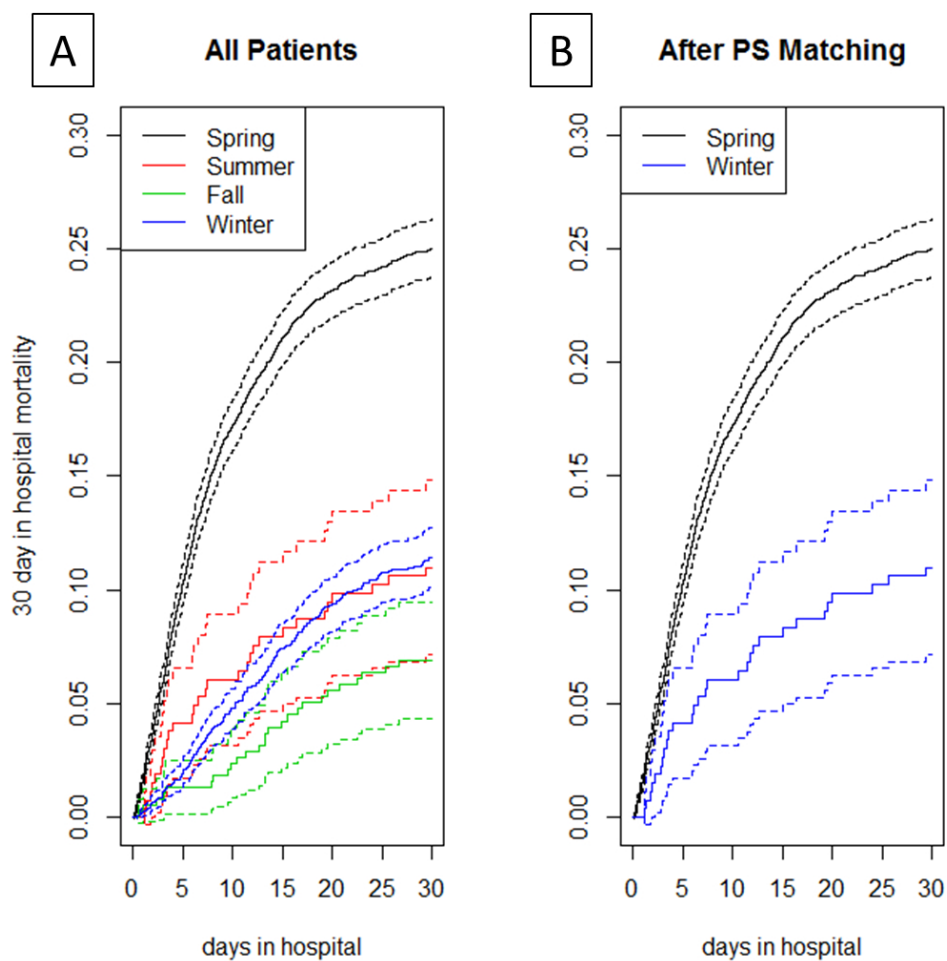


Figure 4. Cumulative Incidences  
 30-day in-hospital mortality by seasons.  
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**Supplemental Appendix**

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**Supplemental Table 1 - Comparison Survivors versus Non-survivors**

	Survivors (n=5953)		Non-survivors (n=1437)		p-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	5953	64 (52 - 75)	1437	73 (65 - 82)	<0.001
Male sex - no (%)	5953	2989 (50.2)	1437	846 (58.9)	<0.001
Black race and / or Hispanic ethnicity - no (%)	5953	4472 (75.1)	1437	1013 (70.5)	<0.001
Body Mass Index (IQR) - kg/m <sup>2</sup>	5679	28.4 (24.6 - 33.2)	1352	27.9 (23.8 - 32.6)	<0.001
Hospital bed saturation (IQR) - %	5953	94.1 (86.5 - 104.8)	1437	99.3 (87.5 - 107.6)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	5953	4365 (73.3)	1437	1169 (81.4)	<0.001
Sleep apnea - no (%)	5953	688 (11.6)	1437	178 (12.4)	0.38
Hyperlipidemia - no (%)	5953	3366 (56.5)	1437	975 (67.8)	<0.001
Atrial fibrillation - no (%)	5953	557 (9.4)	1437	224 (15.6)	<0.001
Chronic kidney disease - no (%)	5953	1559 (26.2)	1437	622 (43.3)	<0.001
Heart failure - no (%)	5953	1181 (19.8)	1437	456 (31.7)	<0.001
Coronary artery disease - no (%)	5953	1653 (27.8)	1437	587 (40.8)	<0.001
Asthma/COPD - no (%)	5953	1842 (30.9)	1437	464 (32.3)	0.32
Diabetes mellitus - no (%)	5953	3168 (53.2)	1437	933 (64.9)	<0.001
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	5926	99 (98 - 100)	1427	99 (98 - 100)	0.35
SBP (IQR) - mmHg	5932	132 (117 - 148)	1430	127 (107 - 146)	<0.001

1	DBP (IQR) - mmHg	5926	76 (67 - 85)	1428	71 (60 - 81)	<0.001
2						
3	HR (IQR) – bpm	5927	96 (83 - 110)	1429	100 (85 - 114)	<0.001
4						
5	Oxygen saturation (IQR) - %	5922	96 (93 - 98)	1430	92 (84 - 96)	<0.001
6						
7	Respiratory Rate (IQR) - bpm	5928	19 (18 - 21)	1428	22 (19 - 26)	<0.001
8						
9						
10	<b>Laboratory Markers</b>					
11						
12	Hemoglobin (IQR) - g/dL	5823	12.9 (11.4 - 14.1)	1408	12.6 (10.9 - 14.2)	0.006
13						
14	Platelet count (IQR) -k/ $\mu$ L	5825	198 (137 - 264)	1408	172 (88 - 246)	<0.001
15						
16	White blood cell count (IQR) - k/ $\mu$ L	5823	6.9 (5.1 - 9.5)	1408	8.3 (6.0 - 11.9)	<0.001
17						
18	Absolute lymphocyte count (IQR) - k/ $\mu$ L	5880	1.1 (0.7 - 1.5)	1423	0.9 (0.6 - 1.2)	<0.001
19						
20	Sodium (IQR) – mEq/L	5879	137 (134 - 140)	1428	138 (134 - 143)	<0.001
21						
22	Potassium (IQR) – mEq/L	5845	4.2 (3.8 - 4.6)	1426	4.4 (4.0 – 5.0)	<0.001
23						
24	Chloride (IQR) – mEq/L	5864	100 (96 - 103)	1423	100 (95 - 104)	0.28
25						
26	Bicarbonates (IQR) – mEq/L	5879	24 (21 - 27)	1428	22 (18 - 25)	<0.001
27						
28	Creatinine (IQR) - mg/dL	5876	1.0 (0.8 - 1.5)	1427	1.6 (1 - 2.9)	<0.001
29						
30	Glucose (IQR) - mg/dL	5879	126 (104 - 179)	1428	156 (121 - 236)	<0.001
31						
32	Aspartate aminotransferase (IQR) - U/L	5416	35 (24 - 55)	1312	52 (33 - 81)	<0.001
33						
34	Alanine aminotransferase (IQR) - U/L	5614	26 (16 - 42)	1376	28 (18 - 46)	<0.001
35						
36	Lactic acid (IQR) – mmol/L	5097	1.9 (1.4 - 2.6)	1347	2.6 (1.8 - 3.9)	<0.001
37						
38	Lactate dehydrogenase (IQR) - mmol/L	4017	384 $\pm$ 219	926	518 (371 - 706)	<0.001
39						
40	Creatine Kinase (IQR) – U/L	4714	336 (253 - 454)	1218	777 $\pm$ 2657	<0.001
41						
42	D-dimer (IQR) - $\mu$ g/mL	3850	1.2 (0.7 - 2.5)	763	2.5 (1.3 - 6.9)	<0.001
43						
44	Procalcitonin (IQR) – ng/mL	2800	0.1 (0.1 - 0.3)	615	0.6 (0.2 - 2.4)	<0.001
45						
46	Troponin T* (IQR) - ng/mL	2365	0.01 (0.01 - 0.03)	302	0.03 (0.01 - 0.1)	<0.001
47						
48	Troponin I* (IQR) – ng/mL	2684	0.01 (0.01 – 0.02)	981	0.02 (0.01 - 0.08)	<0.001
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1	Interleukin-6 (IQR) – pg/mL	1752	17 (6 - 40)	287	68 (26- 154)	<0.001
2						
3	Fibrinogen (IQR) – mg/dL	2478	570 (448 - 690)	460	621 (506 - 761)	<0.001
4						
5	Ferritin (IQR) – ng/mL	3395	521 (224 - 1112)	659	1021 (514 - 2161)	<0.001
6						

7 COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR =  
8 Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I  
9 was available only after June 2020.  
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## Supplemental Methods

### *Covariate Selection Method for Multivariable Competing Risk Proportional Hazard Models for in-hospital Death between Patients Spring and Winter Patients*

The covariates in the multivariable analyses included factors present in > 90% of our dataset, are known to be associated with in-hospital COVID-19 mortality based on prior literature or with a univariate association between admission season (exposure) or in-hospital mortality (outcome) ( $p < 0.05$ ) and a clinical (relative difference >5%) difference between the spring and winter patients (**Supplemental Table 2**). These variables included: age, sex, BMI, vital signs at presentation, white cell count, creatinine, glucose, alanine transaminase, history of hypertension, dyslipidemia, chronic kidney disease (CKD), heart failure, coronary artery disease, asthma/chronic obstructive pulmonary disease, diabetes mellitus and statin use. Also in this model, lactic acid level and percent of hospital bed saturation were forced into the model as marker of illness severity and level of hospital stress, respectively.

**Supplemental Table 2 - Comparison Spring Vs Winter**

	Spring (n=4495)		Winter (n=2254)		P-value
	Sample	Value	Sample	Value	
<b>Demographics</b>					
Age (IQR) - yr	4495	66 (55 - 77)	2254	67 (56 - 77)	0.051
Male sex - no (%)	4495	2377 (52.9)	2254	1122 (49.8)	0.016
Black race and / or Hispanic ethnicity - no (%)	4495	3345 (74.4)	2254	1635 (72.5)	0.098
Body Mass Index (IQR) - kg/m <sup>2</sup>	4229	28.4 (24.6 - 33)	2194	28.2 (24.4 - 33.1)	0.433
Hospital bed saturation (IQR) - %	4495	97.4 (86.5 - 107.6)	2254	95.3 (91.9 - 101.8)	<0.001
<b>Past Medical History</b>					
Hypertension - no (%)	4495	3370 (75)	2254	1713 (76)	0.357
Sleep apnea - no (%)	4495	521 (11.6)	2254	270 (12)	0.640
Hyperlipidemia - no (%)	4495	2609 (58)	2254	1380 (61.2)	0.012
Atrial fibrillation - no (%)	4495	449 (10)	2254	267 (11.8)	0.019
Chronic kidney disease - no (%)	4495	1406 (31.3)	2254	620 (27.5)	0.001
Heart failure - no (%)	4495	980 (21.8)	2254	519 (23)	0.254
Coronary artery disease - no (%)	4495	1316 (29.3)	2254	721 (32)	0.022
Asthma/COPD - no (%)	4495	1371 (30.5)	2254	753 (33.4)	0.015
Diabetes mellitus - no (%)	4495	2522 (56.1)	2254	1244 (55.2)	0.475
<b>Vitals at Presentation</b>					
Temperature (IQR) - F	4463	98.9 (98.2 - 100)	2254	98.7 (98.1 - 99.8)	<0.001
SBP (IQR) - mmHg	4469	131 (114 - 148)	2254	132 (117 - 148)	0.002
DBP (IQR) - mmHg	4465	75 (65 - 84)	2252	75 (67 - 84)	0.117
HR (IQR) - bpm	4467	98 (85 - 112)	2253	95 (82 - 107)	<0.001

1	Oxygen saturation (IQR) - %	4463	95 (91 - 98)	2253	96 (92 - 98)	<0.001
2						
3	Respiratory Rate (IQR) - bpm	4466	20 (18 - 22)	2254	19 (18 - 22)	<0.001
4						
5	<b>Laboratory Markers</b>					
6						
7						
8	Hemoglobin (IQR) - g/dL	4372	12.8 (11.2 - 14.1)	2228	12.9 (11.5 - 14.2)	0.030
9						
10	Platelet count (IQR) -k/ $\mu$ L	4372	188 (116 - 260)	2228	196 (143 - 259)	<0.001
11						
12	White blood cell count (IQR) - k/ $\mu$ L	4372	7.5 (5.6 - 10.6)	2228	6.4 (4.7 - 8.8)	<0.001
13						
14	Absolute lymphocyte count (IQR) - k/ $\mu$ L	4420	1 (0.7 - 1.4)	2246	1 (0.7 - 1.4)	0.062
15						
16	Sodium (IQR) – mEq/L	4414	137 (134 - 141)	2253	137 (134 - 140)	<0.001
17						
18	Potassium (IQR) – mEq/L	4389	4.3 (3.9 - 4.8)	2243	4.1 (3.8 - 4.5)	<0.001
19						
20	Chloride (IQR) – mEq/L	4394	98 (95 - 103)	2253	101 (98 - 104)	<0.001
21						
22	Bicarbonates (IQR) – mEq/L	4414	24 (20 - 26)	2253	24 (21 - 27)	<0.001
23						
24	Creatinine (IQR) - mg/dL	4410	1.1 (0.8 - 2)	2253	1.1 (0.8 - 1.5)	<0.001
25						
26	Glucose (IQR) - mg/dL	4414	134 (108 - 197)	2253	126 (104 - 184)	<0.001
27						
28	Aspartate aminotransferase (IQR) - U/L	4045	40 (27 - 65)	2084	35 (24 - 55)	<0.001
29						
30	Alanine aminotransferase (IQR) - U/L	4206	27 (17 - 44)	2171	26 (17 - 44)	0.292
31						
32	Lactic acid (IQR) – mmol/L	3981	2.1 (1.6 - 3)	1913	1.9 (1.4 - 2.5)	<0.001
33						
34	Lactate dehydrogenase (IQR) - mmol/L	2935	384 (285 - 535)	1563	341 (254 - 468)	<0.001
35						
36	Creatine Kinase (IQR) – U/L	3453	168 (83 - 401)	1957	126 (67 - 282)	<0.001
37						
38	D-dimer (IQR) - $\mu$ g/mL	2204	1.8 (0.9 - 3.9)	1907	1.2 (0.7 - 2.3)	<0.001
39						
40	Procalcitonin (IQR) – ng/mL	1789	0.2 (0.1 - 0.9)	1252	0.1 (0.1 - 0.3)	<0.001
41						
42	Troponin T* (IQR) - ng/mL	0	NA	2106	0.01 (0.01 - 0.03)	NA
43						
44	Troponin I* (IQR) – ng/mL	3662	0.01 (0.01 - 0.03)	0	NA	NA
45						
46	Interleukin-6 (IQR) – pg/mL	1056	34 (14 - 75)	710	11 (4 - 26)	<0.001
47						
48	Fibrinogen (IQR) – mg/dL	1552	624 (491 - 750)	1040	536 (434 - 652)	<0.001
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Ferritin (IQR) – ng/mL	1969	716 (335 - 1498)	1637	510 (230 - 1094)	<0.001
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COPD = Chronic obstructive pulmonary disease; DBP = Diastolic blood pressure; HR = Heart rate; IQR = Interquartile range; SBP = Systolic blood pressure. \* Troponin T was available only until June 2020, Troponin I was available only after June 2020.

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**Supplemental Table 3 - Initial Laboratory Blood Tests**

	<b>Spring (n=4495)</b>	<b>Summer (n=264)</b>	<b>Fall (n=377)</b>	<b>Winter (n=2254)</b>
Hemoglobin (IQR) - g/dL	12.8 (11.2 - 14.1)	12.4 (10.7 - 13.9)	13 (11.6 - 14.3)	12.9 (11.5 - 14.2)
Platelet count (IQR) - k/ $\mu$ L	188 (116 - 260)	228 (169 - 300)	200 (144 - 257)	196 (143 - 259)
White blood cell count (IQR) - k/ $\mu$ L	7.5 (5.6 - 10.6)	8 (5.8 - 11)	6.6 (5.1 - 8.9)	6.4 (4.7 - 8.8)
Absolute lymphocyte count (IQR) - k/ $\mu$ L	1 (0.7 - 1.4)	1.2 (0.9 - 1.8)	1.1 (0.8 - 1.5)	1 (0.7 - 1.4)
Sodium (IQR) - mEq/L	137 (134 - 141)	138 (135 - 141)	137 (135 - 140)	137 (134 - 140)
Potassium (IQR) - mEq/L	4.3 (3.9 - 4.8)	4.2 (3.8 - 4.6)	4 (3.8 - 4.4)	4.1 (3.8 - 4.5)
Chloride (IQR) - mEq/L	98 (95 - 103)	103 (100 - 105)	101 (99 - 104)	101 (98 - 104)
Bicarbonates (IQR) - mEq/L	24 (20 - 26)	24 (21 - 27)	25 (22 - 27)	24 (21 - 27)
Creatinine (IQR) - mg/dL	1.1 (0.8 - 2)	1 (0.8 - 1.5)	1 (0.8 - 1.3)	1.1 (0.8 - 1.5)
Glucose (IQR) - mg/dL	134 (108 - 197)	121 (100 - 171)	122 (102 - 173)	126 (104 - 184)
Aspartate aminotransferase (IQR) - U/L	40 (27 - 65)	26 (20 - 38)	31 (21 - 47)	35 (24 - 55)
Alanine aminotransferase (IQR) - U/L	27 (17 - 44)	21 (14 - 32)	25 (16 - 41)	26 (17 - 44)
Lactic acid (IQR) - mmol/L	2.1 (1.6 - 3)	1.9 (1.4 - 2.7)	1.8 (1.3 - 2.5)	1.9 (1.4 - 2.5)
Lactate dehydrogenase (IQR) - mmol/L	384 (285 - 535)	254.5 (196 - 340)	300 (225 - 383)	341 (254 - 468)
Creatine Kinase (IQR) - U/L	168 (83 - 401)	97 (57 - 176)	116 (60 - 213)	126 (67 - 282)
D-dimer (IQR) - $\mu$ g/mL	1.8 (0.9 - 3.9)	1.1 (0.5 - 2.2)	0.8 (0.5 - 1.6)	1.2 (0.7 - 2.3)
Procalcitonin (IQR) - ng/mL	0.2 (0.1 - 0.9)	0.1 (0.1 - 0.4)	0.1 (0.1 - 0.2)	0.1 (0.1 - 0.3)
Troponin T* (IQR) - ng/mL	NA	0.01 (0.01 - 0.03)	0.01 (0.01 - 0.02)	0.01 (0.01 - 0.03)
Troponin I* (IQR) - ng/mL	0.01 (0.01 - 0.03)	0.01 (0.01 - 0.01)	NA	NA
Interleukin-6 (IQR) - pg/mL	33.6 (13.8 - 75.2)	11.7 (3 - 43.1)	11 (4.7 - 22.2)	10.8 (4.3 - 25.6)
Fibrinogen (IQR) - mg/dL	624 (491 - 750)	448 (370 - 583)	540 (436 - 663)	535.5 (434 - 652)

1	Ferritin (IQR) – ng/mL	716 (335 - 1498)	228 (90 - 562)	364 (166 - 785)	510 (230 - 1094)
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5 IQR = Interquartile range. \* Troponin T was available only until June 2020, Troponin I was available only after  
6 June 2020  
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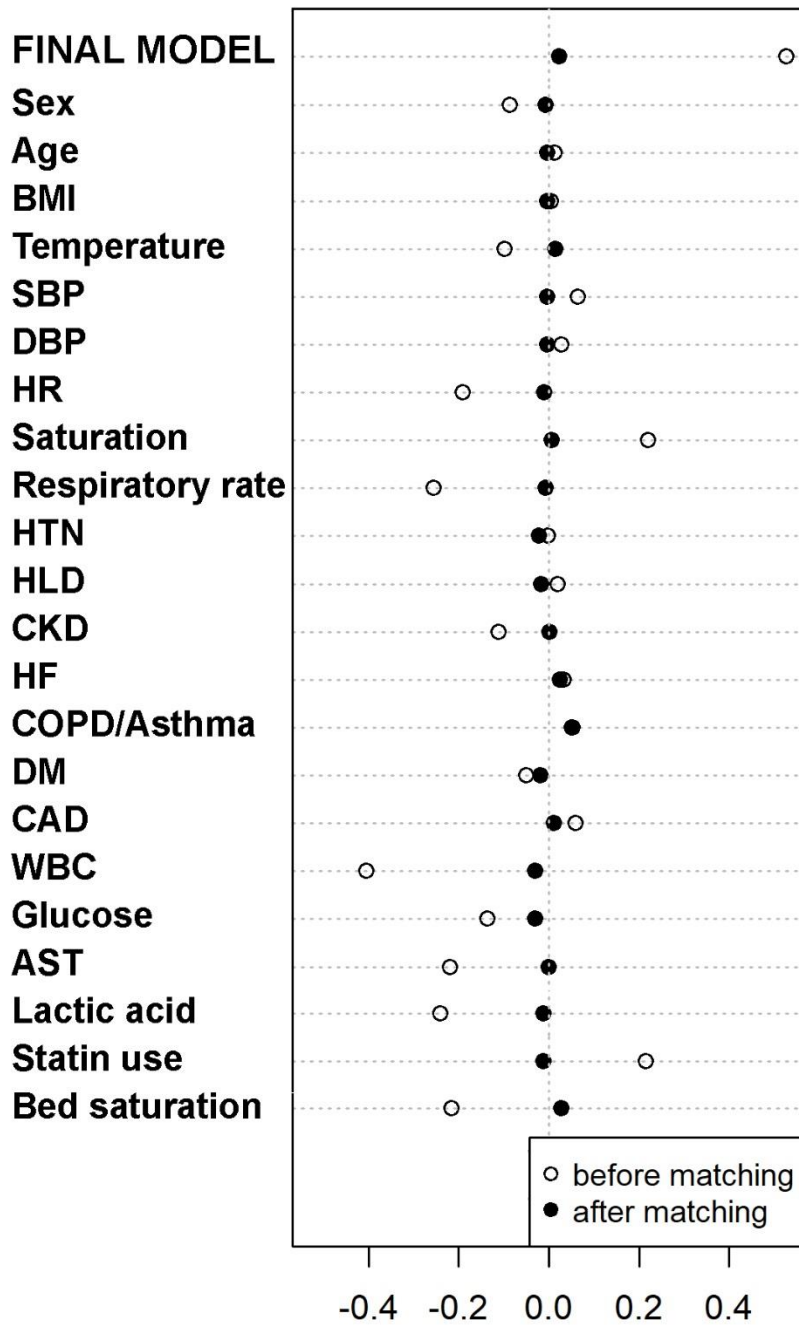
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**Supplemental Table 4 - Therapies Administered during the Admission**

	<b>Spring</b> <b>(n=4495)</b>	<b>Summer</b> <b>(n=264)</b>	<b>Fall</b> <b>(n=377)</b>	<b>Winter</b> <b>(n=2254)</b>
<b>Hydroxychloroquine - no (%)</b>	3007 (66.9)	1 (0.4)	2 (0.5)	8 (0.4)
<b>Azithromycin - no (%)</b>	1322 (29.4)	51 (19.3)	118 (31.3)	374 (16.6)
<b>Other antibiotics - no (%)</b>	3382 (75.2)	160 (60.6)	214 (56.8)	1082 (48)
<b>Steroids - no (%)</b>	1485 (33)	71 (26.9)	195 (51.7)	1462 (64.9)
<b>Angiotensin-converting-enzyme Inhibitors - no (%)</b>	318 (7.1)	36 (13.6)	51 (13.5)	269 (11.9)
<b>Angiotensin II receptor blockers - no (%)</b>	264 (5.9)	23 (8.7)	32 (8.5)	212 (9.4)
<b>Statin - no (%)</b>	1478 (32.9)	109 (41.3)	129 (34.2)	1002 (44.5)
<b>Therapeutic anticoagulation - no (%)</b>	1041/4496 (31.2)	76 (28.8)	98 (26.0)	772 (34.3)
<b>Remdesivir* - no (%)</b>	78 (1.7)	37 (14)	134 (35.5)	1224 (54.3)
<b>Lopinavir/Ritonavir – no (%)</b>	40 (0.9)	0 (0)	0 (0)	0 (0)
<b>Ivermectin – no (%)</b>	11 (0.2)	1 (0.4)	0 (0)	34 (1.5)

\* 45 patients listed as remdesivir recipients in the spring season were part of a 1:1 double-blind, placebo-controlled study. Instead, all the patients in summer, fall, and winter seasons listed as remdesivir recipients received the actual medication.

Supplemental Figure 1 - Distribution of Propensity Score



AST = aspartate transaminase; BMI= body mass index; CAD= coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; DBP= diastolic blood pressure; DM = Diabetes mellitus; HF= heart failure; HLD = hyperlipidemia; HNT = hypertension; HR = heart rate; SBP = systolic blood pressure; WBC = white blood cell count

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 Supp
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12- 13
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	5-6  Supp
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	6-7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	6-9
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-9
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
5	<b>Discussion</b>			
6	Key results	18	Summarise key results with reference to study objectives	9
7	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
8	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
9	Generalisability	21	Discuss the generalisability (external validity) of the study results	14
10	<b>Other information</b>			
11	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.